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THE GENESIS AND RESOLUTION OF PULMONARY TRANSUDATES AND EXUDATES

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The existence of pulmonary edema is one of the first conditions that medical students are sure they have found. Listening to the chest in cases of cardiac decompensation, one hears rales of varying magnitude, and as one progresses toward the bases of the lungs the characteristic signs of edema may be lost. The student, being preternaturally alert, says at once to himself and to nearby nurses "Ah, a pleural effusion!"

Forthwith a new issue arises. To tap or not to tap—that is the question! Having been a medical house officer and a medical resident with a surgical complex, kept under with difficulty, I usually found a reason for trying to drain this abnormal collection of fluid, and when I scored heavily in my collection I was correspondingly gratified. That the fluid in question reaccumulated in a few hours did not bother me. I had done something positive, something which could be shown as action in the attempt to cure a sick patient.

ANATOMY AND PHYSIOLOGY OF THE LUNGS

What, then, can one say as to the reasons why this patient's lungs and pleural sacs filled with fluid and his access to oxygen became less and less?

Let me call attention first to a few bits of anatomy and physiology. The lungs of man are so organized as to provide astonishing ability in the meeting of sudden strains. A healthy young adult can readily increase his pulmonary ventilation from a resting minute volume of 8 liters to 125 liters during exercise, and with this change his cardiac output may rise from 5 liters a minute to perhaps 20 liters a minute.

In spite of this astonishing adaptability, the lungs of man and of mammals are a critically vulnerable link in efficiency in the sense that with each cardiac systole the lungs receive from the right ventricle as much blood as the left ventricle pumps out to the body as a whole. Ordinarily the lungs are not a reservoir of blood, though, if the heart is failing, they may become so. Let us trace the physiology of the development of pulmonary edema, one of the most frequent of clinical experiences.

The lungs possess a blood capacity, in terms of instant cardiac output, equal to that of the entire body. Furthermore, many measurements of the pressure in the pulmonary artery of dogs and cats have been singularly uniform for the species. Also the effects of measures designed to increase the pressure in the pulmonary artery, such as the injection of ephedrine or very considerable augmentation of the blood flow into the heart, cause comparatively little change in pulmonary arterial pressure. These facts mean that in the ordinary course of human experience, when you run up a long flight of stairs in order not to be unduly late for a class or when you find yourself in one of those interminable deuce sets in tennis—when you do not want to go on and cannot stop—your peripheral or general arterial blood pressure rises, but the pressure in the pulmonary vessels is little changed.

No one has measured the pressure in the capillaries of the lungs. It is an intriguing problem. Landis [1] summarized his direct measurements of capillary pressure and all of us know that under continuous intratracheal insufflation with the lungs quiescent but oxygen supply adequate one might measure pulmonary capillary pressure. Yet the figure obtained would not be satisfactory, since the lungs would not be in motion and the negative pressure in the chest, which is a fluctuant factor, would be absent.

I have said that under the usual experiences of exercise in which systemic blood pressure is increased and blood is shunted to the active muscles pulmonary blood pressure rises insignificantly. During the past seventy-five years many investigators have striven to show that the pulmonary circulation is under some sort of vasomotor control. They have not succeeded, and the reason for this failure rests in the very nature of the pulmonary oxygenating mechanism. As far as is possible, the lungs must receive and oxygenate all the blood brought to them. This is accomplished by adjusting the breathing and by letting the increased blood flow spread passively through a capillary bed great enough to carry all the blood that can be sent to it, even under the most extreme conditions of cardiac output. This simple fact is one of the fundamental conceptions of clinical physiology, and we may now attempt to explore its implications.

The problems of the formation of pulmonary exudates and transudates are complicated by our dependence for knowledge on sections of dead lungs. We are almost of necessity preoccupied by what is seen in the alveoli and forget that the fluid which escapes from the blood capillaries must first of all be interstitial, must to a degree at least thicken the alveolar partitions.

Alpha Omega Alpha Lecture read by Dr. Drinker before the University of Virginia Department of Medicine, Charlottesville, Va., Oct. 12, 1942.

1. Landis, E. M.: Capillary Pressure and Capillary Permeability, Physiol. Rev. **14**: 404, 1934.

which normally are just great enough in cross section to contain the pulmonary capillaries and nothing else. Even the lymphatics do not extend into the alveolar wall past the very beginning of the respiratory portion, the atrium. It is clear that any foreign material in the alveolar wall must interpose a barrier to exchange of gas. I believe this fact was first thoroughly, or better generally, appreciated at the time of the initial gas attack in the last war, when the Germans used chlorine at Ypres. Obviously, an increase in the interstitial fluid of the lungs cannot long remain out of the alveoli, and with alveolar and bronchiolar filling by transudate or exudate the individual is progressively separated from his air supply.

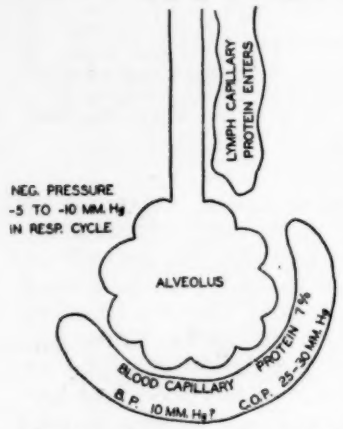

Fig. 1.—Diagram of alveolus, blood capillary and lymphatic in the mammalian thorax.

Let us return now to normal matters. On account of the vast extent of the pulmonary capillary bed and the great elasticity of the lung tissue, it is probable that the pressure in the pulmonary capillaries is low—let us guess around 5 to 10 mm. of mercury instead of 20 mm. of mercury for typical systemic capillaries. The colloid osmotic pressure of the blood going through the lungs is, however, normal and much higher than the capillary blood pressure. The situation to be discussed is shown diagrammatically in figure 1.

Clearly the arrangement found in the lungs makes for dryness. The hydrostatic pressure, tending to force fluid and solutes out of the blood capillaries, is probably well below the osmotic pressure of the blood proteins, which causes absorption of water. It would seem that if the capillaries of the lungs resembled those in other parts of the body there would be little leakage of proteinized fluid from the capillaries and consequently no normal use for the lymphatics of the lungs. But hardly any essential part of the mammalian body has a more profuse supply of lymphatic vessels, and, especially in man, lymphoid tissues—both unorganized collections of lymphocytes and more significantly definite lymph nodes—are extraordinarily numerous.

In 1940 we [2] isolated the lymph drainage from the heart of the dog, collected cardiac lymph and showed that the flow and composition of this lymph could readily be correlated with such straightforward factors as increased cardiac output and anoxia. As is so often the case, during active experimentation other possibilities were evident—lymphatics near the cardiac vessel—and it seemed that these must have come from the lungs. It was a welcome sight, since long before a whole year had been spent in trying to collect lymph from the lungs. A few times a bloody fluid was secured, which was certainly lymph but which had been rendered highly abnormal by the clumsiness of our operative approach.

Today it is easy to collect lymph from the lungs alone, but to do it with absolute certainty the anterior mediastinum must be opened under artificial respiration. There is an alternative to this formidable operation: If the right lymphatic duct is cannulated under natural breathing one obtains pulmonary and cardiac lymph. In an experiment in which anoxia is avoided and cardiac output is shown to remain constant or to fall, it is reasonable to assume that increase in lymph flow from the right duct comes from the lung or is the result of experimental manipulations aimed at the lungs alone. The anatomy essential to support this conclusion is shown in figures 2 and 3. In figure 2 [3] the heart and great vessels are shown from the front. The right lymphatic duct enters the right subclavian vein above a lymph node, which is quite constant in position. Two other nodes are found between the superior vena cava and the aorta. The lymphatics in this chain drain the heart and lungs and enter the right lymphatic duct. For simplicity the vessels involved are shown singly, but a number of afferent lymphatics enter each node. With experience one learns to distinguish the smaller cardiac lymphatic passing to the upper node from the numerous lung vessels. Figure 3 shows the lymphatics of the lungs from the rear; it is clear that drainage from both lungs goes to the right lymphatic duct. Only the upper part of the left lung supplies lymph to the thoracic duct.

A final point relative to the right duct in the dog is the fact that in at least half the animals in which the right duct has been cannulated chyle has flowed freely from it. This fact has not been realized by the biochemists who have attempted to measure fat absorption by means of thoracic duct lymph, since in many cases an almost equal amount of chyle enters the blood on the right side and has been interpreted as direct blood absorption of fat.

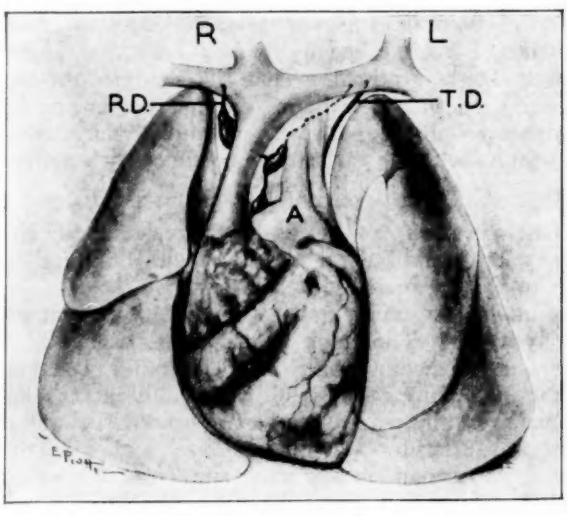

Fig. 2.—The lymphatic drainage of the lungs of the dog, showing the heart, lungs and great vessels viewed anteriorly. The superior vena cava is the prominent landmark. On the right there is a single node not far below the subclavian vein. To the left of this vessel two other nodes are usually found, and from the upper one an inconstant vessel may occasionally cross to the thoracic duct.

THE FORMATION OF TRANSUDATES

From what has been said it is easy to see that in studying the formation of pulmonary transudates and exudates two methods of attack may be employed. In

2. Drinker, C. K.; Warren, Madeleine F.; Maurer, F. W., and McCarrell, Jane D.: The Flow, Pressure and Composition of Cardiac Lymph, Am. J. Physiol. **130:** 43 (July) 1940.

3. Warren, Madeleine F.; Peterson, Delores K., and Drinker, C. K.: The Effects of Heightened Negative Pressure in the Chest, Together with Further Experiments on Anoxia in Increasing the Flow of Lung Lymph, Am. J. Physiol. **137:** 641 (Nov.) 1942.

many dogs the right lymphatic duct may be cannulated without opening the chest and the output of the heart and the oxygenation of the blood followed constantly. If these things are done and the lymph from the right duct does not contain chyle, what one collects comes,

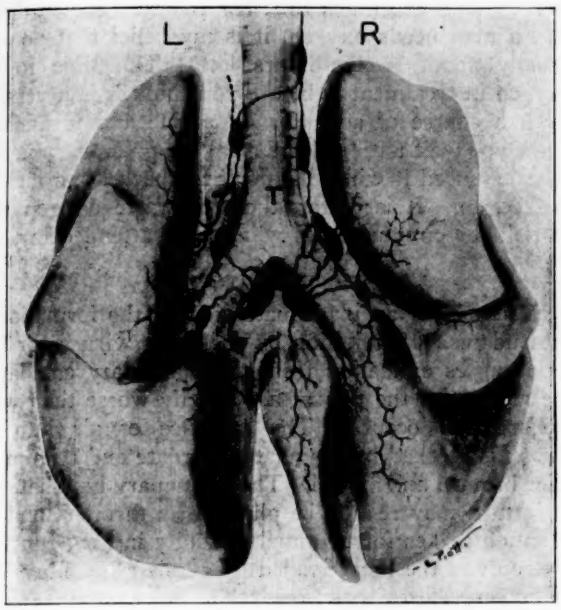

Fig. 3.—Illustrating a fact found in almost all cases—that lymph from the lungs drains ultimately to the right side. It is a rear view of the lymphatic system and lungs of the dog.

in the main, from the lungs and represents practically the total lung delivery at the moment.

In order to follow the production of pulmonary transudates I shall start with a simple experiment. In figure 4 such an attempt is shown. In this case the right lymphatic duct was cannulated and the lymph found chyle free. Through a tracheal cannula the dog, anesthetized with soluble barbital, breathed pure oxygen against no resistance. At the end of an hour and a half lymph flow from the right duct was 11 mg. a minute and, as is usual, contained a few red blood cells. The breathing was then shifted, by turning a three way valve, so that inspiration was made difficult by cotton wool resistance. At the height of inspiration intrathoracic negative pressure reached 56 mm. of mercury. The flow of lymph increased at once and the lymph became bloody.

This seems like an obvious finding, but it happens to be particularly important today, when many of us are working on different sorts of masks without much knowledge of what abnormal resistance to breathing may accomplish. In 1933 Yamada [4] made pleural punctures on several hundred normal Japanese soldiers. He obtained fluid from 29 per cent of his subjects, if they had been at rest, and from 70 per cent following severe work. The lesson of this observation and of our experiments rests in the fact that severe respiratory movements, which increase negative pressure in the chest, will tend to produce pleural and pulmonary exudates even if oxygen lack is avoided, and anoxia, as you shall see, is another potent cause of pulmonary edema. Yamada's observations are, I think, common to us all. Who of you have failed to notice that, if you push yourselves too hard physically, you begin to cough and what you bring up is a watery salty fluid which is not disagreeable; but you know it is not normal and you have extended yourself too far.

In a person with cardiac decompensation there often develops a collection of fluid in the pleural sacs, and with this collection there are abundant signs that his lungs are soggy from extravascular fluid. These situations are thought of as being due to increased pressure in the pulmonary vessels. I doubt this explanation. I have often increased pressure in the pulmonary capillaries by gradual compression of the pulmonary veins, but this has been done in normal animals with entirely healthy hearts. One can readily force excessive leakage of fluid in the course of such experiments, but the right ventricle is capable of sustaining high pressures for some time and so forces fluid out of the capillaries rather slowly. In the usual case of cardiac decompensation, with valvular heart disease, matters progress gradually. Consider whether dyspnea constantly tending to draw fluid from the pulmonary capillaries by increased negative pressure in the chest, together with progressive anoxia, is not an important feature of the situation and an element in the clinical problem which should be combated by every means in one's power. Cardiac dyspnea is an exhausting and distressing experience but one which the physician rarely thinks much of treating until it is pronounced. It is, as I have indicated, capable of adding to the fluid in the lungs and pleural sacs.

At the same time there is usually anoxia, which is so important for altering the permeability of the pulmonary capillaries toward increased leakage. This matter of anoxia as an element in the production of

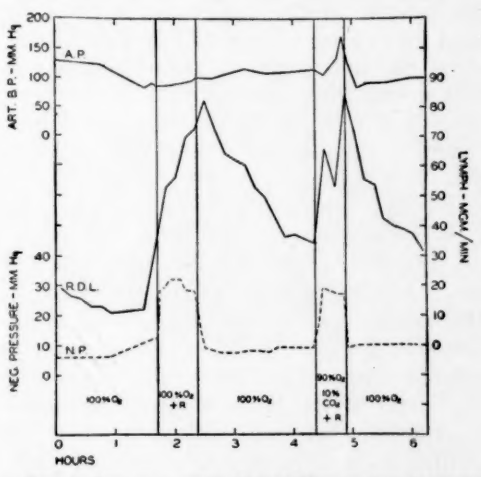

Fig. 4.—Lymph flow as a result of breathing against inspiratory resistance. Upper curve (*A. P.*) indicates arterial pressure; middle curve (*R. D. L.*), lymph from the right lymphatic duct in milligrams per minute; lower curve (*N. P.*), negative pressure in the chest. Lymph flow became 11 mg. a minute after an hour and a half of unresisted breathing. When inspiration was impeded by cotton wool resistance, lymph flow rose to 82.5 mg. a minute. On removal of resistance, flow fell but again increased when resistance was reimposed and 10 per cent carbon dioxide was added to the oxygen in order to force maximal inspiratory efforts. (From Warren, Peterson and Drinker.[3])

pulmonary edema has been easy to explore experimentally. The chest of a dog is opened by removing the upper part of the sternum down to the third ribs, which are cut. This exposure brings the base of the

4. Yamada, So Sabro, and assistants: Ueber die seröse Flüssigkeit in der Pleurahöhle der gesunden Menschen, Ztschr. f. d. ges exper. Med. **90:** 342, 1933.

heart into view and the top of the upper lobes of the lungs. It is not a radical opening of the chest and leaves the lungs well covered and the heart undisturbed. Under these circumstances, which require artificial respiration, one may collect lymph during ventilation with pure oxygen and then shift suddenly to ventilation

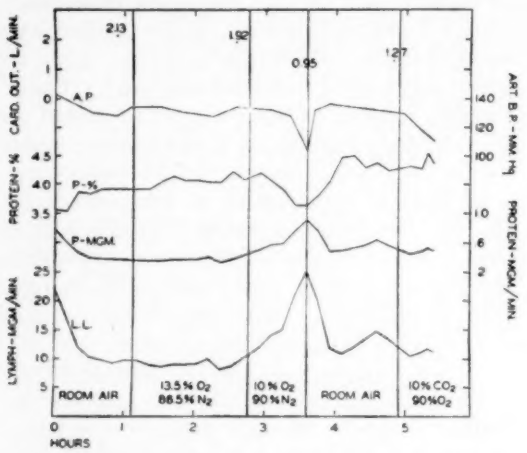

Fig. 5.—The flow of lymph from the lungs when alveolar oxygen is lowered. Dots with figures, cardiac output in liters per minute; upper curve shows arterial blood pressure; second curve, protein in lung lymph in percentage; third curve, protein in lymph from the lungs in milligrams per minute; fourth curve, milligrams of lymph from the lungs per minute. Between the vertical lines, the animal received gas mixtures as shown, the rate and stroke of the respiration pump being always uniform. (From Warren, Peterson and Drinker.[3])

with oxygen poor mixtures. In order to prevent any tendency to respiratory movements during periods of oxygen lack, the animals may be curarized in addition to the complete soluble barbital anesthesia. The results are shown typically in figure 5. In this instance ventilation of the animal with air was first instituted. In this experiment lymph flow from the lungs became steady at 9.7 mg. a minute. Under these circumstances the oxygen content of the blood was 16.08 volumes per cent and the cardiac output 2.13 liters a minute. With the same rate and stroke of the respiration pump the ventilation was then changed to 13.5 per cent oxygen and 86.5 per cent nitrogen. Cardiac output fell to 1.92 liters a minute and the oxygen content of the blood to 9.48 volumes per cent. This change did not increase lymph flow or alter lymph protein concentration. When, however, ventilation was made 10 per cent oxygen and 90 per cent nitrogen, lymph flow rose at once. Cardiac output fell to 0.95 liter a minute and the oxygen saturation of the arterial blood became 4.23 volumes per cent. This very low figure could not be endured long. The interesting point is not that the capillaries of the lungs leaked considerably under these conditions but that, just as soon as ventilation was shifted back to room air, lymph flow fell at once to the figure which existed before the reduction in oxygen began.

This is an important and sensitive indication of the way in which very acute oxygen lack causes increased free fluid in the lungs. It should be noticed too how quickly adequate oxygen in the ventilating air stopped a pernicious process. When oxygen lack causes the pulmonary capillaries to begin to leak, the very fact of increased fluid in the lung tissues, and even more in the alveoli, cuts down the ease of passage of oxygen into the blood capillaries.

The clinical implications of these findings are sufficiently obvious. The capillaries of the lungs are in a unique position. They gain their oxygen from the air, not secondarily from the blood. From what I have had an opportunity to see experimentally, I believe that clinically we fail to appreciate the patient's need for oxygen until too much time has passed. If you decide that a man needs oxygen, it is my belief that you are usually about twelve hours late. The time to use oxygen in treatment is before you think it is necessary. Such a course of action is expensive and formidable, but if you wait until leakage from the pulmonary vessels is pronounced it will be difficult to check the cycle that has begun. It is better, then, to waste oxygen than to risk the circumstances which may attend delay.

EXUDATES

So much for an inadequate view of the formation of transudates. If irritation by chemicals, viruses or bacteria causes exudation from the pulmonary capillaries, the results for the patient are usually worse than when transudation occurs. The entrance of air into the alveoli is blocked by coagulated exudate and cells in the finer bronchi and alveoli. The pulmonary lymphatics in their turn may readily be plugged by thrombi, and the situation makes for maximal difficulty in lung function. Not only is the lung flooded by exudate but fibrin formation interferes with removal of the exudate. When clotting occurs in and about an area of inflammation, healing takes place either wholly or partially by scar formation. This may do relatively little harm in many parts of the body, but in the lungs there is inevitable loss of function.

Solution of the exudate and removal of small molecules through vascular absorption is the most efficient and rapid means of clearing the lungs of exudates. If the irritant does not destroy cells extensively, coagulation of the exudate may be slight, and in this case it

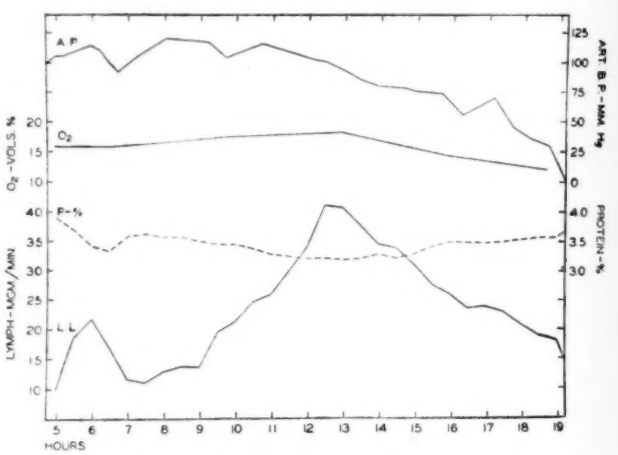

Fig. 6.—The flow and composition of lymph from the lungs in a dog given 45 parts per million of chlorine for thirty minutes three hours prior to the beginning of the record. The initial increase in lymph flow is due to obstruction and manipulation during the operation. The real changes due to chlorine began eight hours after administration of the gas. Upper curve (*A. P.*), indicates arterial blood pressure; second curve (O_2), oxygen in arterial blood; third curve (*P*), lymph protein in percentage; fourth curve (*L. L.*), lymph flow in milligrams per minute.

will drain steadily through the lymphatics. In all parts of the body the lymphatics carry away substances from the tissues which as such are not absorbable by the blood capillaries. Most notable of these are the blood

proteins, which leak in slight amounts from the capillaries practically all over the body, exceptions being found in the renal glomeruli, the choroid plexuses and the capillaries of the ciliary body. From the lungs, as has been shown in figures 2, 3, 4 and 5, lymph flows continuously. It contains 2 to 3.75 per cent of blood proteins and clots, but clotting does not occur in the lung tissue or lymphatics unless irritation has been severe enough to kill cells and release thromboplastic material.

As in the case of lymph movement all over the body, motion of the lungs is extremely important for causing lymph flow. A quiescent lung produces almost no lymph from large collecting trunks, and what little can be garnered is due to the pulsation of the pulmonary vessels.

The lungs are peculiarly adapted to absorb water by virtue of their vast capillary bed. Colin [5] in 1873 gave 21 liters of water to a horse intratracheally in three and one-half hours without the slightest detriment to the animal. When one considers the low hydrostatic pressure in the pulmonary capillaries and the comparatively high colloid osmotic pressure of the blood proteins, it is not surprising that this is the case. The lungs are thus beautifully organized to rid themselves of excess water unless, as is particularly apt to occur in young patients with mitral stenosis and with an abnormal resistance to flow of blood through the lungs, transudates are formed and, as a result of the increased pressure in the alveolar capillaries, water cannot be absorbed.

If the lungs of a healthy anesthetized dog are irritated with chlorine in an amount which would be fatal if the animal was permitted to recover from the anesthetic, a curious series of events ensues. Using 45 parts per million of chlorine for half an hour, one notices no change in lymph flow or composition for about eight hours (fig. 6). In this experiment the chest of the animal is opened and ventilation by air is provided by a pump which operates uniformly. The result is a very vivid expression of the way in which certain lung irritants act. Examinations of patients and trials on animals have shown that after a number of sorts of gassing there is a period of varying length in which the victim is quite normal. This does not take place if the gas is too concentrated, but in the case of common offenders —nitrogen dioxide, chlorine and phosgene—the individual may have breathed a fatal dose of the gas, but his dangerous symptoms do not appear for some time.

The dog in this experiment drowned in a pulmonary exudate which did not begin to accumulate significantly until eight hours after the gassing. This exudate eventually clotted, owing to cell damage, as one can readily see in sections of the lung. Coagulation not only fixed fluid in the alveoli and bronchi but clogged the lymphatics, so that from every angle the animal was fatally assailed.

How can such conditions be treated? It is an interesting fact that blood continues to pass through the lungs even under the worst situations. That is, even though the lung capillaries are caused to leak freely they do not fail to conduct blood. What fails is oxygenation of the blood. You can assist this by giving pure oxygen to breathe instead of air, and even more so by placing such patients in pure oxygen under one or two atmospheres of pressure. Perhaps other therapy may help, but essentially these patients need oxygen, for the changes which have been caused by the irritant gas produce oxygen lack in a steadily mounting form. This is the essential physiologic problem, and the only way to combat it is by the early use of pure oxygen and even by the use of oxygen under pressure. There is no efficient way of getting oxygen into the body except through the lungs, and if the barrier between alveoli and blood has become abnormal the pressure of the oxygen in the lung air must be increased so as to force it in.

5. Colin, G.: Traité de physiologie comparée des animaux, ed. 2, Paris, J.-B. Baillière et Fils, 1873, vol. 2, pp. 109 and 110.

CONCLUSION

I should like to point out that, though I have spoken quite positively, my remarks have dealt mainly with experiments. Consider them as yeast which may rise as ideas in your minds and lead to facts.

Dr. Folin, the greatly distinguished and intrepid biochemist at Harvard, believed that scientific advance arose through the devising of new methods. In many respects he was right, but method, as Pasteur expressed it, save that he used the word "chance," awaits "the prepared mind." The difficulty with experimental advance resides in finding the combination of the "prepared mind" and the technical skill necessary for the experiment. In the issues I have pictured, it is certain that direct experiments may be done. There can be no doubt that the pulmonary lymph reflects rapidly in the living animal changes which will be fatal if they are not resisted. It is a continuous expression of change in the lungs as against the deductions which may be drawn from the sacrificed or dead animal. Equally true is the fact that different measures for combating pulmonary edema and pulmonary exudates may be examined in progressive physiologic experiments such as I have described and do not require the depressing finalities of the autopsy table to give one a poor idea of the way to combat a familiar clinical entity.

This is the message I wish to leave with you: Well conceived and adroitly accomplished mammalian experiments may mean much to human therapeutics. But make no mistake; experiments on mammals are supremely difficult. Very often the experimenter sees surprising and arresting things, but ever and always he should ask himself whether what he has observed is the way in which the animal has reacted against the technical mistreatment of the experiment or whether it is a significant truth the results of which may be applied to the diagnosis and treatment of disease.

55 Shattuck Street.

Treatment of Gas Gangrene.—Once gas gangrene is established, the most drastic treatment must be employed. The general principles are the same as those on which prophylaxis is based: radical excision of all damaged muscular, cellular, integumentary and other tissues. Owing to the spread of the infection in a longitudinal upward direction and its rapid passage from the initial focus through the whole muscle and then to the adjoining muscles, gangrene sometimes spreads from the thigh to the trunk in less than twenty-four hours. It is therefore vital that treatment should be carried out before the infection has passed beyond its localized stage. Four weapons are available against an established infection: surgical operation, antiserums, chemotherapy and deep x-ray therapy.—Trueta, Joseph: The Principles and Practice of War Surgery, St. Louis, C. V. Mosby Company, 1943.

TRICHINOSIS AND PERIARTERITIS NODOSA

DIFFERENTIAL DIAGNOSIS; POSSIBLE RELATIONSHIP

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Although differential diagnostic difficulties seldom arise in cases of "typical" acute trichinosis, the problem is not so simple in mild, subacute, chronic or otherwise unusual ones, which comprise the majority of cases.[1] Hall [2] lists about fifty diseases or conditions which have been mistaken for trichinosis, yet neither he nor most authors include periarteritis nodosa as one of them in spite of its clinical resemblance to trichinosis. On the other hand, trichinosis is often mentioned with dermatomyositis and other obscure conditions in discussions of the differential diagnosis of periarteritis nodosa. In fact, numbers of cases of periarteritis nodosa have been recognized by the typical histologic lesion at biopsy in cases of suspected trichinosis. In diseases as similar to each other and as variable in their manifestations as trichinosis and periarteritis nodosa, it is surprising that no mention is made in any of the reports we have read of serious problems in differentiating them. Differentiation seems to resolve when clearcut evidence eventually develops in one direction or the other. However, since about 16 per cent of the general population has asymptomatic trichinosis,[3] the possibility or likelihood of the two diseases occurring in the same patient must be considered. It is even possible that one may cause the other. Early diagnosis is important because of the difference in the two diseases of prognosis and of epidemiologic management.

Problems in diagnosis which may arise in trichinosis or periarteritis nodosa and evidence of the possible relationship of the two diseases are illustrated in the following reports:

REPORT OF CASES

CASE 1.—*History.*—C. P., a laborer aged 35, had had asthmatic attacks since November 1939, which gradually became worse but never interfered with his work. In December 1940 he "caught a cold," which obliged him to go to a hospital for several days for severe asthma. A brief attack of watery, bloody diarrhea occurred. He recovered, but early in February 1941 severe coughing, dyspnea, occasional hemoptysis and anorexia developed. On February 14 "intestinal grip" with watery, bloody diarrhea recurred and lasted several days. Pain developed in his calves, ankles and feet, with tingling and numbness. During this time there were chilliness, night sweats, vomiting, diarrhea, paroxysms of coughing and lacrimation with pain and burning. He was admitted to the hospital six days later complaining of chilliness, night sweats, anorexia and weakness. He had lost 11.3 Kg. (25 pounds) in two months.

On admission to the hospital the patient was seriously sick, was pallid and had a temperature of about 38.9 C. (102 F.). There were conjunctivitis, edema of the lids and periorbital tissues, and a flame shaped hemorrhagic area in the left retina. The heart and the lungs, except for sibilant "asthmatic" rales in an emphysematous chest, were apparently normal. The liver and spleen were palpable. Lymph nodes in the epitrochlear region were slightly enlarged and one was excised for study. The calves and ankles were painful on movement and tender to pressure but otherwise appeared to be normal. The patellar reflexes were hyperactive. The blood pressure was 130 systolic and 70 diastolic.

The hemoglobin and erythrocytes were normal in amount. The leukocytes numbered 11,000, of which 30 per cent were eosinophils. The sedimentation rate of erythrocytes was increased, with almost complete settling in twenty minutes. A small amount of blood flecked sputum was raised during asthmatic attacks in which eosinophils comprised 28 per cent of the leukocytes present. Jaundice was not revealed by the van den Bergh test, and the spinal fluid was normal. Urinalysis showed 2 plus albumin and granular casts, the blood urea nitrogen measured 9.5 mg. per hundred cubic centimeters and the urea clearance was 166 per cent of normal. Serologic tests for syphilis gave negative results. The stool contained occult blood but no parasites. Evidence of emphysema, acute tracheobronchitis and possibly pneumonia was seen in a roentgenogram, but the heart was normal in size. An electrocardiogram showed no abnormality. In tests for hypersensitivity the patient's skin reacted positively to wheat, ragweed pollen and plantain pollen and was weakly positive to feathers and house dust.

Fig. 1.—Fibrinoid necrosis of the media and intima causing partial occlusion of a vessel in fat tissue surrounding a lymph node. Diffuse inflammation of vascular and perivascular tissue. Hematoxylin and eosin, × 200.

Because of the onset with diarrhea, periorbital edema, conjunctivitis, a retinal hemorrhage, pain and tenderness in the calves and eosinophilia, a tentative diagnosis of acute trichinosis was made. The patient on questioning said that for months he had regularly eaten hurriedly cooked hamburger or pork sausage sandwiches and other meats in quick lunch places. Splenomegaly could not then be accounted for; asthma and nephritis were thought to be unrelated conditions.

Course of the Disease.—An irregular temperature, reaching 38.3 C. (101 F.) on occasion, persisted for over five months, after which it was lower but still touched 37.8 C. (100 F.) in July. Bloody diarrhea recurred for several days in February; transient lymphadenopathy occurred in the left axilla and at intervals severe asthmatic attacks. The general condition became worse until April, when gradual improvement began despite evidence of progressive renal failure. The urea clearance diminished from normal to 58 per cent in five months. There were persistent 2 plus to 3 plus albuminuria, granular casts and occasional erythrocytes in the urine. The leukocytes were always increased in number, often as high as 20,000. Eosinophilia ranged from 12 to 46 per cent. The pains and

From the Departments of Medicine and Pathology, Jefferson Medical College and Hospital.

1. Wright, W. H.: A Consideration of the Clinical and Public Health Aspects of Trichinosis, Journal-Lancet **62**: 389-393 (Nov.) 1942.
2. Hall, M. C.: Studies in Trichinosis: III. The Complex Clinical Picture of Trichinosis and the Diagnosis of the Disease, Pub. Health Rep. **52**: 539-551 (April 3) 1937.
3. Kerr, K. B.; Jacobs, Leon, and Cuvillier, Eugenia: Studies on Trichinosis: XIII. The Incidence of Human Infection with Trichinae as Indicated by Postmortem Examination of 3,000 Diaphragms from Washington, D. C., and Five Eastern Seaboard Cities, Pub. Health Rep. **56**: 836-855 (April 18) 1941.

numbness in his legs decreased but the patellar and achilles reflexes disappeared. Bilateral foot drop and slight atrophy of the quadriceps muscles resulted from what probably was peripheral neuritis. Anemia with 60 per cent hemoglobin and 3,000,000 erythrocytes was present. He returned to his home in July 1941.

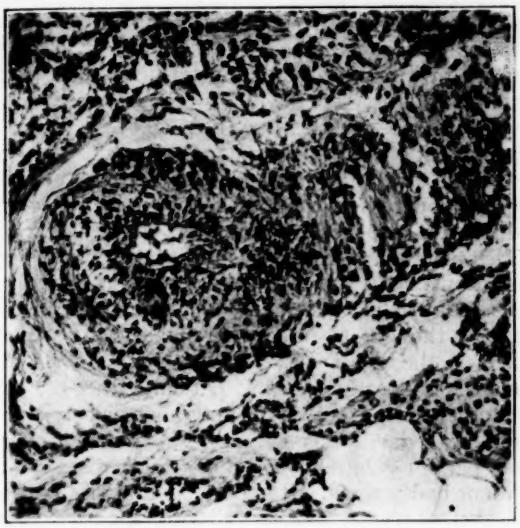

Fig. 2.—Occlusion of a vessel in striated muscle by extensive intimal proliferation. There is panarteritis and periarteritis. The intima contains a giant cell. Hematoxylin and eosin, × 200.

He was fairly well until January 1942, when sudden severe dyspnea forced him to return to the hospital. The temperature rose to 38.9 C. (102 F.) and returned to normal in a week. The leukocytes numbered 27,000; 11 per cent were eosinophils. During this time the asthmatic attacks and cyanosis were most severe, requiring epinephrine and oxygen for control. He improved and was discharged.

Reexaminations were made in February and October 1942. During the spring and summer he improved and returned to work. He was weak, tired easily and had dyspnea on exertion and occasional pains in the wrists or ankles. The blood pressure

Fig. 3.—Hyalinization of some muscle fibers, ballooning and cystlike formation in others. The infiltrating cells are plasma cells, lymphocytes and polymorphonuclear leukocytes. Hematoxylin and eosin, × 200.

gradually rose to 170 systolic and 115 diastolic. He had no asthma until August but had to stop working in October because of the severity of the attacks. The attacks were relieved with ephedrine or epinephrine. By this time the evidence of renal and cardiac failure had become pronounced. There were pretibial edema, pulmonary congestion, hepatomegaly, splenomegaly, leukocytosis, eosinophilia, albuminuria and persistent hypertension. The urea clearance was 30 per cent of normal. An electrocardiogram showed a normal tracing. Biopsy of the pectoralis major and gastrocnemius muscles was made.

The patient's condition in April 1943 remained about the same.

Biopsy Reports.—In the lymph node removed at biopsy in March 1941 there were areas of inflammation about most of the blood vessels, particularly at their bifurcation. The intima and media of many of the arteries showed fibrinoid necrosis so severe in places as to occlude them with débris (fig. 1). The vessel walls were diffusely invaded by polymorphonuclear leukocytes, plasma cells, eosinophils, lymphocytes and erythrocytes. The periarteritis, polyarteritis and panarteritis strongly suggested periarteritis nodosa. In the parenchyma of the lymph node the follicles were almost entirely displaced with cells of the same kind.

In a section of muscle excised from the gastrocnemius at the same time the blood vessels were involved by a similar but more severe process. The entire arterial wall was invaded and the lumen was almost occluded by proliferation of the intima (fig. 2). Occasional nuclei in the intima were heaped together to form giant cells. The perivascular inflammation extended for varying distances into the surrounding connective tissue. In addition there were areas of focal myositis, in no apparent relation to vessels, which showed extensive hyaline degeneration

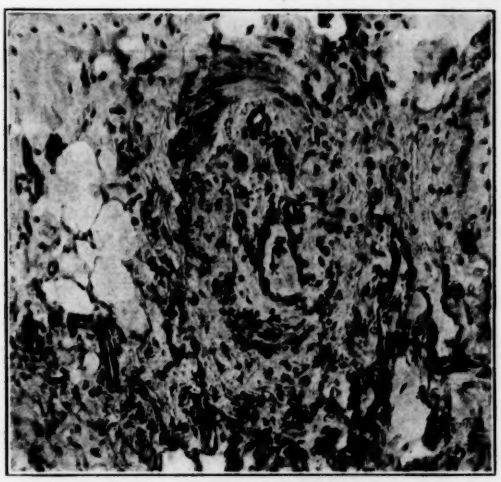

Fig. 4.—Vessel in striated muscle showing remnants of the media at the upper and lower poles. The entire wall, particularly the intima, is fibrotic. Capillaries have canalized the occluded lumen. The vessel wall and perivascular tissue are infiltrated with lymphocytes and plasma cells. Hematoxylin and eosin, × 200.

of the fibers. In places, many of the fibers resembled thin pink shells of tissue or cysts distended with large plasma-like cells (fig. 3). Similar cells together with polymorphonuclear leukocytes and erythrocytes infiltrated the adjoining fibers and connective tissue. The balloon-like areas resembled those which ordinarily enclose trichinella larvae, but no larvae were found and no eosinophils were present.

In a section of muscle removed several weeks later a number of vessels were extensively fibrotic, especially in the intima, as if healing was in progress (fig. 4). Occluded lumens were canalized. Traces of inflammation remained as a few plasma cells, lymphocytes and pigmentary remains of previous extravasations of erythrocytes. Ten months later arteritis had disappeared, leaving fibrous thickening of many vessels. There were extensive fibrosis, scattered leukocytes and free and phagocytosed pigment in the perivascular tissue. In sections from the pectoralis major and gastrocnemius muscle made twenty months later in November 1942, all abnormalities, vascular or otherwise, had vanished except for a few lymphocytes and plasma cells about an occasional vessel.

Specific Tests.—A specimen of blood serum examined in February 1941 by Dr. Sandground of the Lilly Research Laboratories gave a positive precipitin test with trichinella antigen in a titer of 1:800. A second specimen tested by Dr.

Wright of the National Institute of Health was positive in a titer of 1:640. Intracutaneous tests made on several occasions with different antigens supplied by Dr. Sandground and Dr. Wright were negative, as was a complement fixation test. A precipitin test performed by Dr. Wright eleven months later, in January 1942, was positive in a dilution of 1:1,280, but a test in our laboratory in February 1942 was negative. In October 1942 both precipitin and complement fixation tests (Dr. Wright) were negative. A cutaneous test gave rise to an erythematous area 5 mm. in diameter at twenty-four hours.

As stated previously, trichinosis was strongly suspected because the patient ate poorly cooked pork for months. The illness apparently began acutely with bloody diarrhea and fever, followed by pains in his calf muscles, periorbital edema, leukocytosis and eosinophilia; the microscopic evidence was suggestive and precipitin tests with trichinella antigen were positive in high dilution. Only the absence of trichinellae in the muscles, the negative cutaneous tests and complement fixation reaction weakened the diagnosis. Such discrepancies, however, are common in trichinosis. Restudy of muscle tissue, on the other hand, strongly suggested periarteritis nodosa. Nevertheless trichinosis, being the more common disease, was still favored, since even though trichinellae were not seen in the muscle

Fig. 5.—A vessel in striated muscle seen in figure 6. The intima and inner media show massive fibrinoid necrosis with almost complete occlusion of the lumen. The diffuse inflammatory reaction consists chiefly of eosinophils and polymorphonuclear leukocytes. Hematoxylin and eosin, × 200.

inflammatory changes such as were present may occur in adjoining muscle fibers and connective tissue [4] and thrombophlebitis [5] has been recorded.

As the disease progressed over many months the points in favor of a diagnosis of periarteritis nodosa seemed to gain weight, particularly the history of asthma commencing at the age of 33 and persisting; the prolonged, irregular, relapsing fever; lymphadenopathy; splenomegaly; eosinophilia; nephritis, neuritis and the periarteritis, polyarteritis and panarteritis. Yet prolonged fever, pseudoparalysis, splenomegaly, asthma, albuminuria and cylindruria may occur in the course of trichinosis.[6] Asthma, however, antedated the disease described by many months. The pain in the legs, tingling, numbness and foot drop seemed more likely to be the result of neuritis, not myositis. The periorbital edema may have been related to nephritis.

Study of the patient in October 1942, nearly two years after the onset of illness, revealed no clinical, microscopic or serologic evidence of either disease but only a progression of the nephritis and cardiac failure, which are common terminal events of periarteritis nodosa.

Several possibilities may be suggested to account for the patient's illness: (1) periarteritis nodosa, of which the acute stage had passed, leaving lesions which healed or disappeared, with the exception of the renal ones, which are progressive; (2) repeated infections with Trichinella or chronic trichinosis with unusual manifestations, since the precipitin test is supposedly reliable as a confirmatory test [7] and negative cutaneous tests, usually thought to be more reliable, do not necessarily exclude the diagnosis; (3) both trichinosis and periarteritis nodosa in the same patient, either one preceding the other, or (4) an underlying allergic condition, which may be regarded as definite, since many members of the patient's family had "allergic" diseases and the patient had asthma. It is possible that trichinosis, which is also characterized by allergic manifestations, may have aggravated the existing condition or even caused it and brought about the microscopic reaction and subsequent disease regarded as periarteritis nodosa.

CASE 2.—*History.*—P. C., a man aged 38, a Korean born in the Orient, was admitted to the hospital in November 1941 complaining of pain in the calves and shoulders, weakness and loss of weight. In August pain in the neck, shoulders and lumbar and sacral regions lasted for several days in each area and disappeared in about four weeks. Pain then developed in one and then in the other knee, which became red, hot and swollen. This subsided in two weeks, to be followed by arthritis of both ankles, enforcing rest in bed. Soon the muscles of both calves became tender and painful, which made walking impossible for a time and overshadowed other pains and aches. There was also pain in both masseter muscles. These pains lasted about six weeks and gradually subsided. There was residual stiffness of the shoulders and legs, particularly in the morning. There had been occasional night sweats for five weeks and loss of 7.2 Kg. (16 pounds). Obstinate constipation developed.

During the early part of the summer the patient did not feel well and was said to have had anemia, for which he ate large amounts of raw beef and raw pork. The patient, like many Koreans, had eaten poorly cooked meats most of his life. He had had sinusitis for twenty years.

On physical examination the patient was thin but in no apparent distress. The scleras and conjunctivas were inflamed and the lids were edematous. The ocular fundi were normal. There was severe chondritis of the auricle of the right ear, and both drums were reddened. Thick pus containing Staphylococcus albus was present under the turbinate bones, and there was roentgenographic clouding of the frontal, ethmoid and maxillary sinuses. The heart and lungs were apparently normal. The spleen and liver were palpable.

The extremities, including the reflex reactions, were normal except for thinness and tenderness of both calves. There was tenderness and pain on motion of the shoulders and elbows.

The hemoglobin was 68 per cent; the red cells numbered 3,400,000 and the leukocytes 8,000, of which 68 per cent were polymorphonuclear cells, 26 per cent lymphocytes and 6 per cent

4. Hemmert-Halswick, A., and Bugge, G.: Trichinen und Trichinose, Ergebn. d. allg. Path. u. path. Anat. **28:** 313-392, 1934. Tyzzer, E. E.: Trichinosis, in Cecil, R. L.: Textbook of Medicine, ed. 5, Philadelphia, W. B. Saunders Company, 1940, p. 480.

5. Faust, E. C.: Trichinosis, in Musser, J. H.: Internal Medicine, ed. 3, Philadelphia, Lea & Febiger, 1938, p. 309.

6. McCrae, Thomas, in Osler: Modern Medicine, Philadelphia, Lea & Febiger, 1925, vol. 2, p. 590. Blumer, George: Trichinosis, with Special Reference to Changed Conceptions of the Pathology and Their Bearing on the Symptomatology, New England J. Med. **214:** 1229-1235 (June 18) 1936. Wyrens, Tillisch and Magath.[7] Hall.[3]

7. Wyrens, R. G.; Tillisch, J. H., and Magath, T. B.: Trichinosis: Report of Nineteen Cases of Clinical Infection and Twenty-One Cases of Asymptomatic Infection, J. A. M. A. **117:** 428-432 (Aug. 9) 1941.

eosinophils. The sedimentation rate in December and in February was rapid with complete settling in thirty minutes. The Wassermann and Kahn reactions of the serum gave negative results. Urinalysis showed 2 plus albumin, no erythrocytes and a few granular casts. A blood culture was sterile.

Because of a history of having eaten raw pork, painful calf, masseter and other muscles, palpebral edema and eosinophilia,

Fig. 6.—A group of vessels diffusely infiltrated with inflammatory cells near their bifurcation in striated muscle. There is extensive fibrillation of the internal elastic membrane. Elastic tissue stain, × 40.

trichinosis seemed most likely as a diagnosis, but splenomegaly and evidence of nephritis, as in case 1, again raised the question of periarteritis nodosa. Chronic purulent sinusitis was obvious.

Course in the Hospital.—The patient was observed for five months. The temperature was irregular, reaching 38.3 C. (101 F.) occasionally for a month, after which it subsided coincident with improvement of the sinusitis resulting from drainage and irrigation. It frequently reached 37.5 C. (99.5 F.) but became normal two weeks before he left the hospital. The conjunctivitis disappeared. Inflammation of the auricle of one ear gradually healed but later involved the other. The blood pressure was labile, ranging irregularly from 110 systolic and 60 diastolic to 170 systolic and 130 diastolic but was usually 130 systolic and 70 diastolic. The arthralgia and myalgia lessened considerably after a week or two, but the left wrist on one occasion became painful, tender, swollen and hot for several days.

In December a group of papules 3 to 5 mm. in diameter appeared in a small area on the scrotum to which attention was attracted by itching. A portion was excised for biopsy. The blood count remained rather constant, the proportion of eosinophil cells ranging from 1 to 18 per cent.

The urine throughout gave evidence of nephritis with persistent 2 plus to 3 plus albuminuria. A few leukocytes and granular casts were constantly present. The urea clearance at this time was 74 per cent of norma' but progressively decreased to 14 per cent and 9 per cent in three months. The general condition, the myalgia, arthralgia and sinusitis improved so that the patient returned to his home in February, although he was weak and anemic in spite of hematinic treatment. He had regained 9 pounds (4.1 Kg.).

He returned to the hospital after four weeks complaining chiefly of dyspnea, restlessness, insomnia and vomiting. There was general anasarca and purulent nasal discharge. Uremia was evident. The anemia had increased but no eosinophil cells were seen. The urea clearance test was 8 per cent of normal. The blood pressure was 190 systolic and 140 diastolic. He lapsed into coma and died after a convulsion on May 3. The clinical diagnosis was trichinosis, chronic glomerulonephritis, chronic sinusitis and uremia. The histologic diagnosis from biopsy was periarteritis nodosa.

Biopsy Reports.—In December tissue from the gastrocnemius muscle showed diffuse infiltration of the blood vessel walls and perivascular areas with eosinophils, polymorphonuclear leukocytes and occasional plasma cells and lymphocytes. Most of the vessels were occluded by proliferation and fibrinoid necrosis of the intima and inner layers of the media (fig. 5). Diffuse hemorrhagic extravasations but no aneurysmal dilatations were seen. As in case 1, the reaction was especially severe at the bifurcation of vessels. There was abundant fibroblastic proliferation in the perivascular connective tissue. Elastic tissue stain revealed extreme fibrillation of the internal elastic membrane (fig. 6) and slight patchy hyalinization of the muscle fibers. There were no focal areas of myositis dissociated from the vessels and no trichinella larvae were found. The lesions were typical of those of periarteritis nodosa.

Tissue from the scrotal papule showed superficial ulceration of the epithelium. The underlying dermis was rich in engorged, thin walled capillaries, fibroblasts, eosinophils and occasional polymorphonuclear and plasma cells. Vessels not near the ulcers were unchanged. The nature of the lesion was essentially like that in the muscles.

Necropsy Report.—Six months later at necropsy careful search revealed no evidence whatever of either active lesions or healed scars of periarteritis nodosa in the heart, aorta, lungs, spleen, adrenal glands, liver, gallbladder, pancreas, gastrointestinal or urinary tract or vertebral bone marrow. Encysted trichinella larvae, however, were present in the pectoralis major muscle (fig. 7). There was no inflammation or calcification about them and the arteries in the muscle appeared normal. The brain was normal except for evidence of toxic effects on the ganglions, and an occasional artery or vein was surrounded by a loose collection of small monocytes. The nasal sinuses contained no pus, but the lining membranes were thickened. The sphenoid sinus had ruptured into the pituitary fossa, but the latter was not inflamed. Death was evidently caused by chronic glomerulonephritis with acute exacerbation. Glomerular lesions, tubules containing cellular casts and patchy infiltration of the interstitial tissue were present. The arteries, however, were remarkably free from inflammation and even from such sclerosis and fibrosis as are ordinarily present in chronic glomerulonephritis.

Specific Tests.—Because of the clinical impression of trichinosis, blood serum was sent to Dr. Wright for precipitin tests in December 1941. The test was positive in a dilution of 1 : 1,280. Blood taken in February 1942 was again sent to

Fig. 7.—Encysted Trichinella spiralis larva in pectoralis major muscle. Note the absence of inflammation and calcification. Hematoxylin and eosin, × 200.

Washington, where the test was reported as negative, but a sample of the same serum tested by Dr. Sandground was reported positive in a titer of 1 : 800. Cutaneous tests made on three occasions with intradermal injections of different antigens supplied by Dr. Sandground and by Dr. W. H. Wright in December, January and February 1942 all gave negative results. A complement fixation test performed with trichinella antigen also supplied by Dr. Sandground gave a negative result.

The diagnostic problem was similar to that in case 1. Although the so-called acute "primary" stage of trichinosis was not seen or recorded, the history of a lifelong custom of eating undercooked pork makes the infection with Trichinella spiralis very likely. The additional large amounts of deliberately eaten raw pork just before the onset of illness may have induced a reinfection to which the patient reacted in a manner different from the so-called classic case.[2] The painful shoulder and masseter muscles, the recurrent arthritis characteristic of a late stage of trichinosis called "trichinal rheumatism," prolonged fever, periorbital edema, conjunctivitis and eosinophilia all pointed to that diagnosis. As in case 1, the enlarged spleen and evidence of nephritis added a degree of diagnostic confusion which was heightened by the histologic changes of periarteritis nodosa in the muscle. Additional diagnostic factors in favor of periarteritis nodosa were the prolonged febrile period, arthritis and eventual death in uremia. Asthma never occurred. At the time it was thought that the spleen may have been enlarged from preceding forgotten or unrecognized disease during residence in Korea, and the chronic nephritis may have followed the chronic purulent sinusitis or may have been related to trichinosis. Again as in case 1 several precipitin tests for Trichinella were strongly positive, but all specific cutaneous tests and a complement fixation test were negative. The precipitin test on one occasion was reported as positive from one laboratory and negative from another.

Trichinellae were indeed found at necropsy, but no evidence, present or past, of periarteritis nodosa was found even in the kidneys, in which only the changes of commonplace chronic glomerulonephritis were present. The spleen, palpable during life, was normal in size and structure. The presence of Trichinella larvae in the muscles, of course, proved the diagnosis of trichinosis. But the typical microscopic lesions of periarteritis nodosa seen during life, with nephritis terminating in death, are unaccounted for except as (1) a possible result of chronic purulent sinusitis, (2) an unusual, hitherto undescribed reaction in trichinosis, (3) manifestations of periarteritis nodosa occurring as a separate disease during trichinosis, the evidence of which disappeared before death, or (4) trichinosis inciting the microscopic reaction and syndrome known as periarteritis nodosa.

COMMENT

It is obvious that during certain periods of either trichinosis and periarteritis nodosa the similarities between them may be so great as to make clinical diagnosis impossible without the demonstration of Trichinella in the 1 case or of widespread microscopic evidence of active, subsiding or healed lesions of periarteritis nodosa in the other. In certain cases, as in those described, when evidence of both conditions is present, the matter is indeed complex. In both cases described, the clinical diagnosis was trichinosis yet the microscopic diagnosis during life was periarteritis nodosa.

Albuminuria or renal failure in either patient could not be regarded as secondary to trichinosis of the myocardium and heart failure with no evidence therefor. Chronic nephritis more likely caused heart failure. Albuminuria and casts have been recorded in cases of trichinosis. Asthma, as case 1, is an especially common symptom in periarteritis nodosa, but it may also occur in trichinosis.

In both cases described the contradictory results of various specific tests for trichinosis are confusing. It is generally believed that the cutaneous test is more reliable than the precipitin test, but even it may be misleading. Particularly confusing are the results in case 2, in which Trichinella was present in the muscles, yet the cutaneous test, the complement fixation test and on one occasion the precipitin test gave negative results.

Recovery from trichinosis is the rule, but periarteritis nodosa is supposedly a fatal disease. There is, however, reason to believe that healing and recovery may occur at times if the damage done is not too great. Recovery probably happens more often than is realized, but the disease may be unrecognized unless a biopsy is made. According to studies at necropsy, patients have recovered from the acute stage of periarteritis nodosa but died from nephritis or heart failure, and remnants or scars of extensive vascular disease or healed infarcts in various organs have been described.[8] In case 1 nephritis exists but arteritis, present early in the disease, vanished except for a few traces after twenty months. In case 2 death was caused by nephritis, but arteritis was not found at necropsy.

POSSIBLE RELATIONSHIP OF TRICHINOSIS AND PERIARTERITIS NODOSA

With asymptomatic trichinosis present in an estimated 16 per cent of the population [3] there is reason to expect periarteritis nodosa as a separate, unrelated disease in an occasional infected person.[8a] A patient with periarteritis nodosa may likewise contract trichinosis. Yet in both cases described here evidence of a causal relation of trichinosis to periarteritis nodosa is persuasive. In case 1, regarded clinically as one of trichinosis, microscopic changes suggested a progression of lesions, first of trichinosis, later of periarteritis nodosa and then of healing and final disappearance. In case 2, unquestionably one of trichinosis, lesions of periarteritis nodosa were present during life but no remains of them were found at necropsy. Progressive renal failure occurred in both. It is probable that in both trichinosis was the primary factor which initiated the vascular lesions and the clinical syndrome known as periarteritis nodosa, probably through the obscure mechanism of allergy, and that the progressive renal impairment was the result of the vascular injury. Certain cases of chronic nephritis of obscure origin may also be explained on this basis. According to experimental studies trichina antigen is excreted in the urine for weeks after infection of monkeys.[8b] Chronic trichinosis or repeated reinfections give a prolonged opportunity for the development of antibody and its interaction with the antigen.

The possibility that Trichinella spiralis or other nematodes may serve as one of the causes of, or may initiate the onset of, periarteritis nodosa was suggested twenty-five years ago,[9] but in no other report of the latter have we found mention of evidence of trichinosis

8. Spiro, P.: Zur Kenntnis des Wesens der Periarteritis nodosa, Virchows Arch. f. Path. Anat. **227**: 1, 1919. von Haun, F.: Pathohistologische und experimentelle Untersuchungen über Periarteritis nodosa, ibid. **227**: 90, 1919. Arkin, A.: A Clinical and Pathological Study of Periarteritis Nodosa, Am. J. Path. **6**: 401-426 (July) 1930. Schottstaedt, W. E. R.: Periarteritis Nodosa with Remission of Symptoms, California & West. Med. **36**: 186-188 (March) 1932. Weir, D. R.: Polyarteritis Nodosa: Report of a Case, Am. J. Path. **15**: 79-88 (Jan.) 1939. Blaisdell, E. R., and Porter, J. E.: Healed Stage of Periarteritis Nodosa, New England J. Med. **224**: 1087-1090 (June 26) 1941.

8a. Banowitch, M. M.; Polayes, S. H., and Charet, Richard: Periarteritis Nodosa: Report of Five Cases, Ann. Int. Med. **16**: 1149-1179 (June) 1942.

8b. Welt, L. G.: Urinary Excretion of Trichina Antigen in Experimental Trichinosis, Proc. Soc. Exper. Biol. & Med. **48**: 587-589 (Dec.) 1941.

9. Haythorn, S. R., and Ryan, A. H.: Aortic Aneurysm in Dogs with the Report of Six Cases, J. M. Research **35**: 411-423 (Jan.) 1917. Cameron, H. C., and Laidlaw, P. P.: A Case of Periarteritis Nodosa, Guy's Hosp. Rep. **69**: 159-171, 1918.

in studies of tissue. Nevertheless, various allergic manifestations such as asthma, urticaria, edema and eosinophilia common to the two diseases lends credence to the theory.

Periarteritis nodosa is apparently a syndrome of diverse origin. The possibility that it may be a result of hypersensitivity was suggested by Gruber [10] in 1925 and discussed in a recent review by Rich.[11] Rich refers to previous observers who described periarteritis nodosa in patients with serum sickness and adds 5 cases of his own. In further studies he [12] induced the typical lesions of periarteritis nodosa in rabbits by injecting them with horse serum.

CONCLUSION

The 2 cases presented were regarded clinically as trichinosis, yet the typical lesions of periarteritis nodosa were present in tissue examined during life. Both patients had chronic nephritis. One died, and at necropsy no evidence of periarteritis nodosa remained, but trichinellae were found in the muscles. There is a possibility that trichinosis as a disease with strong allergic manifestations may in certain instances serve as one cause of the syndrome called periarteritis nodosa.

LIVER FUNCTION TESTS IN CLINICAL MEDICINE

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Knowledge of the functional status of the liver, gained by the use of tests, is growing in importance in medicine and surgery. Such tests are particularly helpful (1) in patients with jaundice and (2) in some without jaundice as in (*a*) cirrhosis of the liver, (*b*) gallbladder disease, (*c*) controlling the therapy with hepatotoxic drugs and (*d*) hyperthyroidism.

Our object is to give the indications and uses of liver function tests based on our experience gained from examination and study of 563 jaundiced and 112 non-jaundiced patients. In 111 of these cases which came to operation our studies were supplemented by histologic and fluorescence microscopic examination of liver biopsy specimens.

WHICH LIVER FUNCTION TESTS ARE USEFUL?

The answer to the question Which liver function tests are useful? depends first on whether or not the patient is jaundiced.

1. In jaundice, the usual problem is to decide whether it is obstructive or parenchymatous and whether surgical intervention is indicated. Some liver damage occurs in almost every case of jaundice. In parenchymatous jaundice it is usually acknowledged; however, even in obstructive jaundice regurgitated bile may cause liver damage. In the differentiation between obstructive and parenchymatous jaundice, less sensitive liver function tests are indicated—tests which give positive results only if more severe damage to the liver parenchyma is present. In cases of mild hepatitis in which such liver function tests may be negative, the question of surgical intervention usually does not arise.

2. In patients without jaundice, on the other hand, one is often interested in discovering slight deviations of liver function. For such patients the more sensitive liver function tests are needed.

WHAT MAY BE LEARNED FROM LIVER FUNCTION TESTS IN JAUNDICE?

A. *Differentiation Between Medical and Surgical Jaundice Within the First Six Weeks.*—After this period, secondary liver damage due to prolonged obstruction becomes severe enough to produce the same functional changes as in cases of severe primary hepatitis. If, however, after six weeks of jaundice the less sensitive liver function tests still yield negative results, they may be of diagnostic value.

B. *Indications for Immediate Surgical Intervention in Patients with Obstructive Jaundice.*—If during the observation or preparation period of a patient with established biliary obstruction liver function suddenly fails, immediate surgical relief of the obstruction is indicated.

C. *Estimation of the Degree of Liver Damage (or Liver Reserve), Especially in Chronic Liver Disease (as in Cirrhosis).*—The knowledge of the degree of liver damage is important in the evaluation of the therapy.

D. *Prognosis in Acute Hepatitis.*—The course of the disease can be recognized by impairment (danger of acute yellow atrophy) or by improvement of the liver function. The results of liver function tests often indicate improvement before the jaundice has subsided.

WHICH PROCEDURES DIFFERENTIATE BETWEEN MEDICAL AND SURGICAL JAUNDICE?

Because of the inherent difficulties in liver function tests (presence of secondary hepatitis), attention should be given to examination of bile pigment metabolism before function tests of the type of the tolerance tests are used.

Bile Pigment Metabolism.—The endothelial and especially the reticuloendothelial cells of the body form hemobilirubin from hemoglobin. This pigment is probably connected with plasma protein and circulates in the blood but does not pass into the urine. It gives the characteristic diazo reaction (van den Bergh) only after the serum protein has been precipitated with alcohol. Hemobilirubin is taken up by the liver cells and excreted into the bile capillaries as cholobilirubin, which supposedly is freed of the protein connection. In the intestine, cholobilirubin is reduced by bacterial action to urobilinogen (stercobilirubin). Most of the stercobilirubin is excreted with the feces, to which it imparts color, and part of it is reabsorbed into the blood stream and reaches the liver. The liver reoxidizes most of it to bilirubin, which is again excreted in the bile (enterohepatic circulation). Traces of it remain in the blood and appear in the urine (fig. 1 *A*). Normally, traces of urobilinogen and no bilirubin are excreted in the urine.

10. Gruber, G. B. Zur Frage der Periarteritis nodosa, mit besonderer Berücksichtigung der Gallenblasen- und Nieren Beteiligung, Virchows Arch. f. path. Anat. **258**: 441, 1925.

11. Rich, A. R.: The Role of Hypersensitivity in Periarteritis Nodosa as Indicated by Seven Cases Developing During Serum Sickness and Sulfonamide Therapy, Bull. Johns Hopkins Hosp. **71**: 123-136 (Sept.) 1942.

12. Rich, A. R., and Gregory, J. E.: The Experimental Demonstration that Periarteritis Nodosa is a Manifestation of Hypersensitivity, Bull. Johns Hopkins Hosp. **72**: 65-88 (Feb.) 1943.

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Hemolytic jaundice (symptomatic or idiopathic) results from more hemobilirubin being formed. The liver compensates by excreting larger amounts of bilirubin B into the bile. More urobilinogen is formed in the intestine, more is reabsorbed into the blood and more is excreted into the urine (fig. 1 *B*). In hemo-

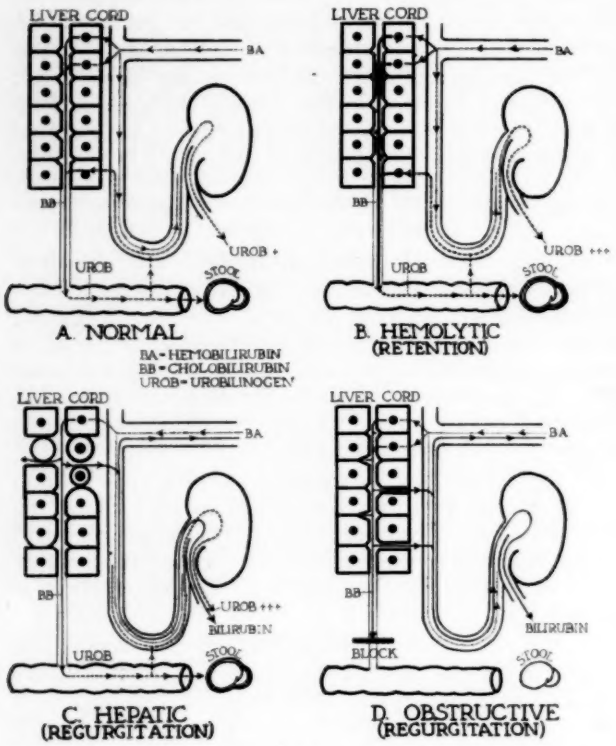

Fig. 1.—Schematic drawing explaining the changes of the bile pigment metabolism in the various forms of jaundice.

lytic jaundice, the urine contains no bilirubin but increased amounts of urobilinogen.

In jaundice with complete obstruction, the cholobilirubin cannot enter the intestine. No urobilinogen is formed and none absorbed into the blood stream. The bile ducts and capillaries above the obstruction dilate and the capillaries may finally rupture, permitting regurgitation of cholobilirubin into the blood stream. Thus cholobilirubin which can pass through the kidney circulates in the blood. In obstructive jaundice, the urine contains bilirubin but no urobilinogen (fig. 1 *D*).

In partial obstruction, as is usually found in cholelithiasis after the first few days, bilirubin is present in the urine while the amount of urobilinogen varies according to the degree of obstruction and may even be increased after release of the obstruction.

In parenchymatous jaundice, necrobiosis of the liver cells causes openings in the bile capillaries through which some cholobilirubin regurgitates into the blood stream. Early in the disease the greater amount of cholobilirubin reaches the intestine, where urobilinogen is formed. Little of the reabsorbed urobilinogen is oxidized by the impaired liver and much of it appears in the urine (fig. 1 *C*). In more severe types, less and less cholobilirubin reaches the intestine, less urobilinogen is formed, less is reabsorbed and, in spite of a damaged liver, less and finally no urobilinogen is found in the urine (intrahepatic obstruction). Hence in parenchymatous jaundice the urine contains bilirubin and much urobilinogen in the incipient and recovery stages but only little urobilinogen in the fully advanced stage.

Test for Bilirubin in the Urine: Overlay 2 to 5 cc. of urine with 1:10 alcoholic dilution of tincture of iodine. A green ring forming at the area of contact indicates bilirubin.

Test for Urobilinogen in the Urine: To 2 cc. of freshly voided urine add 5 to 8 drops of Ehrlich's aldehyde (paramino benzaldehyde in 20 per cent hydrochloric acid) solution. A pink color increasing as the urine is heated indicates normal amounts of urobilinogen. An immediate cherry red color indicates high amounts. A pink color only on heating shows decreased amounts. No color change after heating means absence of urobilinogen. A developing green color is due to bilirubin which has to be removed by adding equal amounts of lime water and 10 per cent calcium chloride solution to the urine and then performing the test on the filtrate. Urobilinogen changes to urobilin on standing. The latter does not give the color reaction. Consequently only freshly voided urine should be used.

A direct reaction to the van den Bergh test has the same significance as bilirubin in the urine, except in cases in which there is severe kidney insufficiency. The more easily performed test for bilirubin in the urine is therefore preferable to the van den Bergh test.

A complete history combined with a careful physical examination and the result of one urinalysis for bilirubin and urobilinogen gave the right diagnosis in 62 per cent of the patients examined. The diagnosis was later proved correct by the follow-up study. This means that in about two thirds of the patients with jaundice one can make the right diagnosis at the bedside or in the office without expensive laboratory equipment.

Two factors particularly were responsible for the failure to diagnose by these simple methods the other 38 per cent: (*a*) the incomplete obstruction due to a stone, which may be associated with secondary hepatitis or with compensating hypersecretion of bile while the

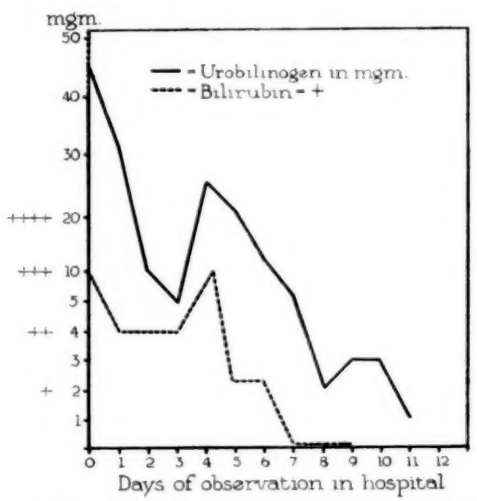

Fig. 2.—Quantitative urobilinogen excretion in twenty-four hours as compared with bilirubin excretion in a case of incomplete obstructive jaundice due to common duct stone.

obstruction is opened, and (*b*) the complete obstruction encountered in certain stages of parenchymatous jaundice, which occurs only in severe hepatitis and usually does not last more than two weeks. The cause of this obstruction is an intrahepatic interference with the bile flow while the extrahepatic biliary passages are intact and not dilated.

In this difficulty some help may be obtained from prolonged observation of the urobilinogen and bilirubin excretion in the urine. This can be done by repetition of the qualitative urinalysis. When possible, however, the quantitative measurement of the excretion of urobilinogen in twenty-four hours (Watson's method [1])

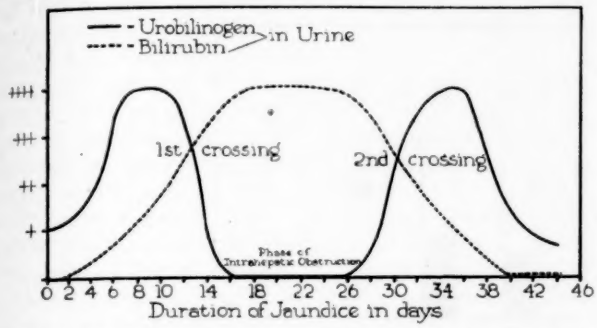

Fig. 3.—Schematic curve of the results of qualitative analysis for bilirubin and urobilinogen in a typical case of parenchymatous jaundice with intrahepatic obstruction.

is preferable, especially if associated with the determination of urobilinogen in the feces. By either of the procedures in incomplete obstruction due to stone daily variations in the amount of urobilinogen will be noted (fig. 2). In parenchymatous jaundice with intrahepatic obstruction a characteristic curve of urobilinogen-bilirubin excretion is obtained by plotting the daily urobilinogen and bilirubin output in the urine. Thus in the initial phase of the disease the urinary excretion of urobilinogen rises and bilirubin appears in the urine. In the following phase, in severe cases, the urobilinogen drops in the face of a rising bilirubinuria (first crossing) (figs. 3 and 4). In the following intrahepatic obstruction phase, none or only traces of urobilinogen and much bilirubin are found in the urine. Recovery is indicated by a gradual rise of the urobilinogen with a drop of the bilirubinuria (second crossing). The prolonged observation of the urinary excretion of the bile pigments increased the percentage of correct diagnoses in jaundice to 79. In the remainder of the cases, the performance of other liver function tests proved useful in the diagnosis.

In the differentiation between surgical and medical jaundice, the following liver function tests were performed in the order of their usefulness:

Galactose Tolerance Test.—Physiology: The liver transforms the carbohydrates of the blood to glycogen and stores it as such. In the event of liver damage, this glycogenesis is impaired. Since other factors may complicate the glycogenesis of dextrose, the transformation of galactose to glycogen is tested. In normal adults, out of 40 Gm. of galactose ingested, enough is stored in the liver so that not more than 3 Gm. appears in the urine (fig. 5). Obviously, in impairment of intestinal absorption, even in the presence of a damaged liver, less than 3 Gm. may be found in the urine.

Technic: [2] The fasting patient empties his bladder and then drinks 500 cc. of water containing 40 Gm. of galactose. Specimens of urine are collected hourly for five hours and those specimens which show sugar on qualitative analysis are lumped together and the sugar is determined quantitatively as for dextrose. The presence of sugar in the urine after five hours makes the result of doubtful value because of the possibility of delayed intestinal absorption.

Oral Hippuric Acid Excretion Test.—Physiology: Ingested sodium benzoate is detoxified by the liver by conjugating it with aminoacetic acid to hippuric acid, which is excreted in urine. Normal liver detoxifies enough of the 5.9 Gm. of sodium benzoate ingested so that hippuric acid equivalent to more than 3 Gm. of sodium benzoate appears in the urine (fig. 5). In contrast to the galactose test, disturbed intestinal absorption will not make the results appear normal. This may be of aid as a check on the absorption of galactose.

Technic: [3] The fasting patient receives a breakfast consisting of two slices of toast and one cup of tea. One hour later he is given 5.9 Gm. of sodium benzoate dissolved in 30 cc. of water followed by half a glass of water. After drinking the water he empties his bladder and then collects the urine for four hours; the hippuric acid is determined on this urine. In renal insufficiency, indicated by nitrogenous retention, the results of this test are doubtful.

Cephalin-Cholesterol Flocculation Test.—Physiology of the Relation Between Liver and Protein Metabolism: The liver influences the concentration of plasma proteins and the constitution of the plasma globulins. In liver damage, the concentration of the plasma albumin decreases while the globulin may remain unchanged or actually increase. The normal albumin/globulin ratio of the plasma is 2:1; it may be changed in chronic liver damage to 1:1 or even become reversed, associated with a general reduction of the total plasma proteins (hypoproteinemia) (fig. 6). Some change of the plasma globulin occurs in acute liver damage. Iontophoresis curves are a scientific but too complicated a method for clinical use.

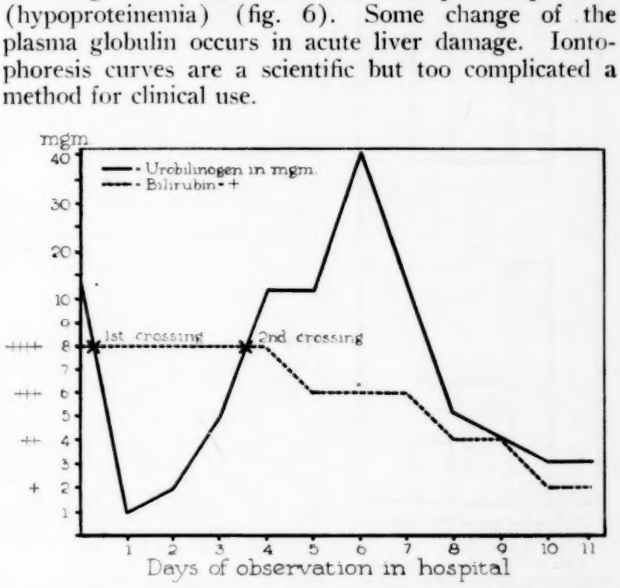

Fig. 4.—Quantitative urobilinogen excretion in twenty-four hours as compared with bilirubin excretion in a patient with parenchymatous jaundice with intrahepatic obstruction of short duration.

The following tests, which can easily be done in the clinical laboratory, indicate essentially the same changes in the plasma globulin: (*a*) cephalin-cholesterol flocculation test in which pathologic globulins flocculate a

1. Watson, C. J.: Studies of Urobilinogen: I. An Improved Method for the Quantitative Estimation of Urobilinogen in Urine and Feces, Am. J. Clin. Path. **6**: 458-475 (Sept.) 1936.

2. Bauer, R.: Ueber die Assimilation von Galaktose und Milchzucker beim Gesunden und Kranken, Wien. med. Wchnschr. **56**: 20-23, 1906. Shay, Harry; Schloss, E. M. S., and Rodis, Isadore: The Galactose Tolerance Test in the Differential Diagnosis of Jaundice, Arch. Int. Med. **47**: 650-659 (April) 1931.

3. Quick, A. G.: Synthesis of Hippuric Acid; New Test for Liver Function, Am. J. M. Sc. **185**: 630-635 (May) 1933. Kraus, Ida, and Dulkin, Sol: Determination of Hippuric Acid in Urine, J. Lab. & Clin. Med. **26**: 729-732 (Jan.) 1941.

cholesterol-cephalin emulsion in various degrees; (*b*) the colloidal gold test in which pathologic globulins precipitate and change characteristically the color of gold chloride; (*c*) Takata-Ara test in which pathologic globulins flocculate an alkaline sublimate solution in serial dilutions.

The early globulin changes in acute hepatitis can be elicited by the cephalin-cholesterol flocculation test and by the colloidal gold test. The Takata-Ara test becomes positive only in chronic liver disease.

The technic of the cephalin flocculation test is described by Hanger.[4] At present the cephalin-cholesterol mixture is available commercially. The test is simple and seems to have particular merits in the presence of jaundice. Because of the danger of false positives, only dense flocculations are significant.

Blood Phosphatase Test.—Physiology: Alkaline phosphatase is an enzyme which splits organic phosphorus compounds in an alkaline medium to inorganic phosphates. It is produced by osteoblasts and consequently it is increased in bone diseases. It is probably excreted through the bile and hence increases in the blood in disturbances of biliary excretion, as seen in extrahepatic obstruction or intrahepatic block of parenchymatous jaundice.

The technic is described by Bodansky.[5] This test is often used in association with the cephalin-cholesterol flocculation test, as they complement each other. A high blood phosphatase level with a high degree of flocculation speaks for hepatitis, while with a low degree of flocculation an uncomplicated extrahepatic obstruction is probable. By itself, however, the phosphatase determination is not of much diagnostic aid, since it possibly indicates only the degree of biliary obstruction, which can be recognized much more simply by the urobilinogen excretion in the urine.

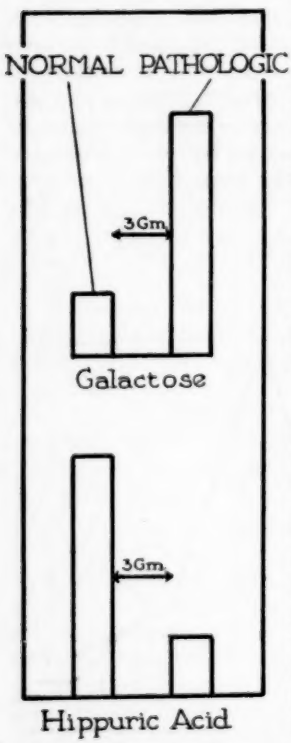

Fig. 5.—Schematic drawing explaining the results of the galactose and hippuric acid tests.

Duodenal Drainage.—By this procedure—which is now much less used than it was previously—one can first note the presence or absence of bile from the duodenum by the color of the duodenal contents. If bile is present, liver bile and the darker gallbladder bile (obtained after duodenal instillation of 30 cc. of a 40 per cent solution of magnesium sulfate) may be obtained separately.

Microscopic examination of the sediment shows many pus cells in the liver bile in cases of cholangitis and in the gallbladder bile in cases of suppurative cholecystitis (empyema). Cholesterol, calcium carbonate and bilirubin crystals, particularly in the gallbladder bile, speak for cholelithiasis. In addition, the excretory function of the liver for dyes can be tested during the duodenal drainage by injecting azorubin S.

Technic for Azorubin-S Test.[6]—Four cc. of a 1 per cent solution of azorubin-S is injected intravenously and 20 cc. of a 40 per cent solution of magnesium sulfate is instilled into the duodenum. Normally a red coloration of the bile appears within twenty-five to thirty minutes. In liver damage the excretion of the dye is delayed or not excreted at all.

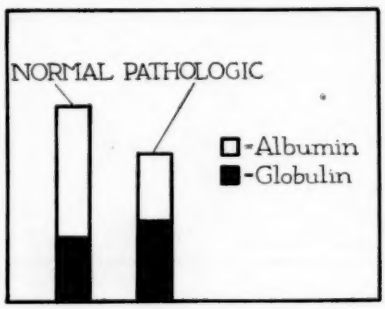

Fig. 6.—Schematic drawing of the relation of the albumin and globulin in the blood serum in normal and pathologic conditions (cirrhosis, nephrosis).

The Colloidal Gold Test.—Physiology: This is discussed under cephalin-cholesterol flocculation tests.

Technic: This is described by Gray.[7] The test seems promising but is somewhat difficult to perform.

Comment.—The application of the liver function tests mentioned raised the percentage of correct diagnoses—as checked by follow-up study, operation or postmortem examination—from 79 to 95 per cent. This indicates that the usefulness of the liver function tests is not as wide as is often assumed. It should be stressed that, despite a rather intensive clinical and laboratory work-up, the right diagnosis was not made in 5 per cent of the cases. During the five years of this study various improvements of the liver function tests were made and their number was increased. Nevertheless, the percentage of failures remained about the same throughout the years.

In analyzing these cases it was found that the chief cause for the failure was that patients with obstructive jaundice first came under observation at a time when secondary hepatitis had already developed. Obviously, impairment of liver function in cases of secondary hepatitis is identical with that in cases of primary hepatitis. Therefore improvement in the liver function tests alone will not decrease the percentage of failures in the differentiation between medical and surgical jaundice. An improvement can be expected only from more accurate clinical observation and care in taking the history. Any improvement of liver function tests would seem to lie mainly in the development of technically simpler procedures.

WHAT CRITERIA POINT TO IMMEDIATE SURGERY IN CASES OF OBSTRUCTIVE JAUNDICE BECAUSE OF IMMINENT LIVER BREAKDOWN?

1. *Increase of the Icteric Index.*—Physiology: In obstructive jaundice, the urinary excretion of bilirubin removes relatively much of the regurgitated bilirubin. Thus after a while a fairly constant bilirubinemia results at an icteric index of 100 to 150. In parenchymatous jaundice, the associated kidney damage reduces the urinary excretion of bilirubin with consequently higher and rising icteric indexes.

4. Hanger, F. M.: Serologic Differentiation of Obstructive from Hepatogenous Jaundice by Flocculation of Cephalin-Cholesterol Emulsions, J. Clin. Investigation **18**: 261-269 (May) 1939.

5. Bodansky, Aaron: Phosphatase Studies: Determination of Serum Phosphatase: Factors Influencing Accuracy of Determination, J. Biol. Chem. **101**: 93-104 (June) 1933.

6. Matsuo, Iwao: Biologischie Untersuchungen über Farbstoffe, Kyoto, The Author, 1935. Rosenberg, D. H., and Soskin, Samuel: The Azorubin S Test of Liver Function: An Evaluation with a Comparative Study of the Bromsulphalein and Hippuric Acid Test, Ann. Int. Med. **15**: 1644-1654 (March) 1940.

7. Gray, S. J.: Colloidal Gold Reaction of Blood Serum in Diseases of the Liver, Arch. Int. Med. **65**: 523-544 (March) 1940.

The sudden rise of the icteric index from a fairly constant level points to a secondary parenchymatous complication.

2. *Falling Prothrombin Level During Administration of Vitamin K.*—Physiology: In jaundice, the intestinal absorption of vitamin K is interfered with owing to the lack of bile acids in the intestine. In liver damage the storage of vitamin K in the liver is additionally impaired. Both factors cause prothrombin deficiency, which may be corrected by administration of vitamin K. In liver damage, however, the formation of prothrombin, even in the presence of vitamin K, is not normal. Therefore, after administering vitamin K to a jaundiced patient the consequent rise of the prothrombin level is prompt and prolonged if the liver is undamaged, whereas in cases of liver damage the rise is only slight and is not sustained.

Technic: The determination of the prothrombin level may be done by the method of Quick [8] and his co-workers or of Smith and his co-workers.[9]

If in a jaundiced patient under observation either the prothrombin level falls or, even worse, hemorrhagic diathesis appears, severe secondary liver damage has developed. That is confirmed by inadequate response to further vitamin K therapy.

3. *Increase of the Nonprotein Nitrogen in the Blood.*—Physiology: The nonprotein nitrogen level of the blood rises in parenchymatous liver damage partly because of increased protein breakdown and more so because of associated pathologic changes in the kidney. The latter is probably on the basis of an inability of the damaged tubular cells to prevent urea reabsorption.[10]

A sudden rise of the nonprotein nitrogen in a patient with jaundice is, therefore, an alarm signal.

4. *Increased Alimentary Galactosuria or Decreased Excretion of Hippuric Acid.*—If, on repetition of these liver function tests, the previously normal results have turned pathologic, the development of a secondary hepatitis is indicated.

5. *Millon's Test.*—Physiology: In severe liver damage increased amounts of amino acids may be present in the blood and thus tyrosine appears in the urine, which is recognized by Millon's reaction.

Technic: Add an equal amount of Millon's reagent [11] to urine and boil. A precipitation develops. A red color of the supernatant fluid indicates the presence of tyrosine. In case of albuminuria, the protein should first be removed from the urine in order to avoid the splitting off of tyrosine from the protein molecule.

WHAT DETERMINES THE DEGREE OF LIVER DAMAGE IN PATIENTS WITH JAUNDICE?

The tests presented here are those in which a somewhat quantitative relation exists between the results of the tests and the degree of liver damage. These relations are especially important in the follow-up of cases of chronic disease and in the evaluation of therapeutic procedures.

1. *Hippuric Acid Excretion Test.*—The amount of hippuric acid excreted is to a certain extent inversely proportional to the degree of liver damage.

2. *Cholesterol-Cholesterol Ester Ratio.*—Physiology: Cholesterol is excreted with the bile; consequently in biliary obstruction the total cholesterol of the blood rises. Supposedly only the liver cells are able to esterify free cholesterol into cholesterol esters. In the presence of a normal liver, two thirds of the total cholesterol in the blood is in ester form (cholesterol-cholesterol ester ratio 1:2). In liver damage the esterification is impaired and consequently independent of the height of the total cholesterol, the ratio is changed to 1:1 or less than 1 (fig. 7).

Technic: A modification described by Kraus was used.[12]

The disturbance of the cholesterol-cholesterol ester ratio is more pronounced the greater the degree of liver damage.

3. *The Albumin/Globulin Ratio.*—Physiology: This is described under cephalin-cholesterol flocculation tests in the section discussing which procedures differentiate between medical and surgical jaundice.

The degree of reversal of the albumin/globulin ratio depends on the degree of liver damage but to a certain

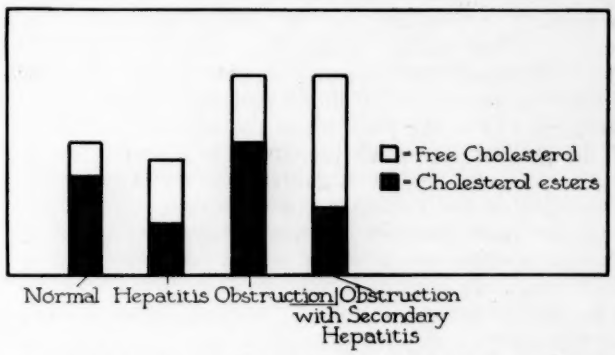

Fig. 7.—Schematic drawing showing the relation between free and esterified cholesterol in normal persons and patients with liver disease.

extent on the development of ascites as well. Nevertheless, the albumin/globulin ratio and the absolute height of the albumin fraction is an especially valuable guide in the follow-up study in cases of cirrhosis.

4. *Cephalin-Cholesterol Flocculation Test.*—The density of the flocculation varies directly with the degree of liver damage.

5. *Takata-Ara Test.*—Physiology: This is described in the section discussing which procedures differentiate between medical and surgical jaundice.

Technic: The method of Jezler [13] was used.

In chronic liver disease the variations in the number of test tubes showing precipitation is in direct proportion to the degree of liver damage.

WHAT INDICATES THE PROGNOSIS IN ACUTE HEPATITIS?

During the course of an acute hepatitis or the course of a superimposed hepatitis in cirrhosis, sometimes a sudden turn for the worse due to breakdown of the liver may appear. The alarm symptoms of an imminent liver necrosis are similar to those of an approaching

8. Quick, A. G.: Determination of Prothrombin, Proc. Soc. Exper. Biol. & Med. **42**: 788-789 (Dec.) 1939.

9. Ziffren, S. E.; Owen, C. A.; Hoffman, G. R., and Smith, H. P.: Simple Bedside Test for Control of Vitamin K Therapy, Am. J. Clin. Path., Tech. Supp. **4**: 13-16 (Jan.) 1940.

10. Meyer, K. A.; Popper, Hans, and Steigmann, Frederick: Significance of Rise of Nonprotein Nitrogen in Medical and Surgical Jaundice, J. A. M. A. **117**: 847-850 (Sept. 6) 1941.

11. One part of metallic mercury is dissolved in two parts of nitric acid (specific gravity 1.42) by gradual heating. After the mercury has dissolved, two parts of water are added.

12. Kraus, Ida, and Kalal, Evelyn: Effect of Standing on Cholesterol and Cholesterol Ester Values in Human Blood, J. Lab. & Clin. Med. **27**: 1208-1211 (June) 1942.

13. Jezler, A.: Beitrag zur funktionellen Leberdiagnostik, Ztschr. f. klin. Med. **111**: 48-70, 1929.

secondary hepatitis in an obstructive jaundice. On the other hand, recovery may be ensuing while the jaundice is still unchanged. Here liver function tests chiefly indicate the dawn of recovery.

Signs of Alarm (Liver Failure).—1. Rise of the icteric index.

2. Millon's test becomes positive.

3. Drop in prothrombin level, only partly relieved by administration of vitamin K.

4. Drop in the cholesterol esters.

5. Rise of the nonprotein nitrogen.

Signs of Recovery.—1. Rise of the urinary urobilinogen in the face of a decrease in the bilirubinuria.

2. Rise of the cholesterol esters.

3. Increased diuresis.

Physiology.—During acute hepatitis the water avidity of the tissues is increased, producing a latent edema. In recovery this stored fluid is excreted. If the daily urinary output is charted, a sudden rise of the diuresis points to improvement.

4. Graham-Cole test becomes negative.

Physiology.—Tetraiodophenolphthalein is excreted into the bile in a concentration which does not give a shadow on roentgen examination of the patient. After concentration of the bile in the gallbladder, the tetraiodophenolphthalein becomes sufficiently concentrated to produce a shadow on the roentgenogram. This shadow is not visible (positive Graham-Cole test) if (1) a damaged liver does not excrete the dye and the kidney excretes it, (2) in obstruction of the biliary passages, (3) in the presence of damage of the mucosa of the gallbladder which interferes with concentration of the bile and (4) if a gallbladder reflex emptying occurs before the roentgenogram is taken.

Generally in jaundice the Graham-Cole test will be positive whether the jaundice is due to hepatitis or to obstruction. In beginning recovery from hepatitis, however, the Graham-Cole test may become negative while some jaundice is still present.

LIVER FUNCTION CHANGES OF DIAGNOSTIC SIGNIFICANCE IN NONJAUNDICED PATIENTS

In the absence of jaundice, slight changes in the liver function from the normal may be significant. In the nonjaundiced patients the more sensitive liver function tests are indicated. There are many conditions in which liver function tests may be of diagnostic or therapeutic help in the absence of jaundice. The four most common situations in which these tests are useful are here discussed.

A. *Early Cirrhosis.*—In a patient with a questionable early cirrhosis the demonstration of slight liver impairment will support the diagnosis.

The following findings are significant:

1. Increased icteric index.
2. Increased urobilinogen in the urine.
3. Bromsulphalein retention.

Physiology.—Bromsulphalein is normally excreted by the liver through the bile. In disturbances of biliary excretion, the blood level after the injection of a test dose remains high. This test is of no use in the presence of jaundice, since both hepatitis and obstruction interfere with the excretion of the dye.

Technic.—Two mg. of bromsulphalein in a 5 per cent solution per kilogram of body weight is injected intravenously and the amount of dye retained is determined by comparing an alkalized serum sample (blood drawn from the other arm thirty minutes later) to standards under the colorimeter. A retention of dye in more than traces is a sign of impaired biliary excretion and of liver damage in the absence of jaundice. The colorimetric readings permit a quantitative estimation.

4. Low albumin fraction and reversed albumin/globulin ratio.

5. Positive Takata-Ara test.

6. Dense flocculation of the cephalin-cholesterol emulsion.

7. Low cholesterol esters.

B. *Chronic Gallbladder Disease.*—In some cases of chronic gallbladder disease without manifestation of jaundice, slight liver damage may be present, as demonstrated by the following tests:

1. Increased icteric index.
2. Bromsulphalein retention.
3. Dense flocculation of the cephalin-cholesterol mixture.
4. Decreased hippuric acid excretion.

C. *In Controlling the Therapy with Hepatotoxic Drugs.*—Following the treatment with certain drugs (arsenicals, cinchophen, sulfonamide compounds and bismuth, among others) hepatitic jaundice may occur. This calls for immediate cessation of the therapy. With some of the drugs, however, especially the arsenicals, continuation of the therapy is sometimes desirable after the jaundice has subsided. Before such therapy is resumed liver function tests should be done to exclude persisting liver damage. In the presence of the latter, the therapy cannot be resumed. The status of liver function should also be determined whenever possible before treatment is started with a drug which may cause liver damage.

The following findings indicate impairment of liver function:

1. Increased urobilinogen in the urine.
2. Bromsulphalein retention.
3. Increased icteric index.
4. Decreased hippuric acid excretion.
5. Dense flocculation of a cephalin-cholesterol emulsion.

D. *Hyperthyroidism.*—In hyperthyroidism impairment of liver function may parallel the degree of thyrotoxicosis. Some[14] feel that the impairment of liver function may serve as an indication of the disease equal to or even more reliable than determination of the basal metabolic rate.

The following tests seem to be useful in evaluating the presence and degree of liver damage:

1. Galactose tolerance test:

In hyperthyroidism there is probably, in addition to liver damage, a faster intestinal absorption of galactose, which may raise the urinary excretion.

2. Hippuric acid excretion test.
3. Bromsulphalein test.
4. Cephalin flocculation test.

In other more rare cases in which liver function tests are indicated in the absence of jaundice, the tests discussed will usually also be of aid.

SUMMARY

Liver function tests according to their usefulness in given situations are indicated in various clinical conditions.

14. Boyce, F. F.: Factors in Mortality of Thyroid Disease in Nonendemic Area; Analysis of 817 Consecutive Surgical Cases and 103 Consecutive Surgical and Nonsurgical Deaths, with Note on Value of Quick Test of Liver Function in Estimation of Hepatic Damage, South. Surgeon **9**: 96-113 (Feb.) 1940.

In the differential diagnosis between surgical and medical jaundice, less sensitive liver function tests are required. In cases of prolonged jaundice the differential diagnosis may be impossible with any type of liver function test owing to the secondary hepatitis in obstructive jaundice. In the presence of jaundice the correct diagnosis can be made in the majority of cases by a good history, careful physical examination and simple qualitative urinary tests.

EMBOLIC ARTERIAL OCCLUSION OF LOWER EXTREMITIES

WITH REPORT OF FOUR SUCCESSFUL EMBOLECTOMIES AND A REVIEW OF THE LITERATURE

CAPTAIN ALBERT LESSER
MEDICAL CORPS, ARMY OF THE UNITED STATES

The early recognition and operative treatment of embolic arterial occlusion of the extremities is still relatively infrequent. With the exception of the work reported by Swedish authors, surgical interest and treatment in this condition has been comparatively scant until very recently. It is significant that Deitch [1] reports only 10 successful embolectomies in Great Britain up to 1936. I, therefore, believe that my recent experiences with 4 successful embolectomies warrants a report of these cases and a review of the subject of arterial embolism of the extremities.

ETIOLOGY

The most frequent cause of arterial embolus in the systemic circulation is a mural thrombus in the left auricle or left ventricle of the heart—in the left auricle as a result of rheumatic heart disease with mitral stenosis or degenerative heart disease with auricular fibrillation and in the left ventricle as a result of cardiac infarction from coronary occlusion. Other possible causes are the so-called paradoxic emboli arising from the peripheral veins or the right auricle and passing through a patent foramen ovale to the left side of the heart; also thrombi arising from the pulmonary veins or from the walls of proximal arteries or aneurysm. These embolic masses may be well organized, hard or even arteriosclerotic plaques; this type usually lodges and remains in one piece. On the other hand, the embolus may be soft and friable, breaking off into many pieces after the original impact with the vessel wall. Emboli usually lodge at the site of bifurcation of major peripheral arteries, blocking both branches. Key,[2] in an analysis of 382 cases, finds the bifurcation of the common femoral artery the most frequent site of embolic obstruction, accounting for 55 per cent of all cases. The 4 cases to be here described occurred in the region of the common femoral or external iliac arteries.

The sequence of conditions occurring immediately following the impact of an embolus on a vessel wall presents an interesting corollary to the symptomatology, prognosis and treatment. A comparison of the embolus with the lumen of the vessel in which it lodges suggests that in many cases the immediate occlusion is due to the intense spasm of the vessel and the regional arterial tree affected. In about two hours, however, there is beginning formation of the distal secondary propagation thrombus. The distal secondary thrombus formation becomes so extensive after nine or ten hours and occludes so many collateral vessel orifices as to prevent return of circulation to an extremity even after operative removal of the embolus. This phenomenon emphasizes the rationale of combating vasospasm by the various measures to be discussed under therapy.

SYMPTOMATOLOGY AND DIAGNOSIS

The symptoms of sudden arterial occlusion are extremely variable and multiple. Severe pain is not always characteristic, and the tendency to look for pain as the chief manifestation of embolism is probably responsible for the frequent failures to recognize the condition early. When pain does occur, it is probably related to the intense arterial spasm of the distal vessel and collaterals, initiated by the sudden impact of the embolus on the vessel wall. Thomas Lewis [3] believes that pain is due to ischemia of the muscles of the extremity involved and is therefore more significant in persons who have recently been active. In bedridden, inactive patients muscle ischemia is not a pertinent factor and numbness and paralysis are more significant symptoms. Pain and tenderness along the course of the embolus and distal propagation clot are only late results. Pain itself may be present anywhere in the limb distal to the site of occlusion. Thus pain in the back would suggest occlusion at the bifurcation of the aorta. The variability of the pain factor is particularly attested in the cases reported in this paper, since all the patients were partially or completely confined to bed for treatment of heart lesions at the time when the acute embolic accident occurred.

Other characteristic findings are absence of the peripheral pulses, a waxy whiteness or blotchy cyanosis of the skin, palpable coldness of the limb, impaired sensation, diminished reflexes and variable degrees of motor paralysis of the limb. A rather striking feature which was observed in my cases was a progressive diminution in the force and amplitude of the femoral pulse in embolism of the common femoral artery; as the hours elapsed a secondary thrombosis completed the extent of the mechanical occlusion of the vessel until the femoral pulse was gradually completely obliterated. De Takats [4] points out that arterial embolism may have premonitory symptoms. A slight degree of numbness, tingling or coldness of the limb may appear days or weeks before the sudden, complete vascular occlusion. These symptoms he believes to be due to the release of minute fragments from the central clot that is about to break loose.

Arterial thrombosis may be a complicating factor either as the original causative agent or as the agent

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1. Deitch, H. I.: Three Arterial Embolectomies in the Same Patient, Lancet **1:** 475-477 (Feb. 29) 1936.

2. Key, Einar: Embolism of the Peripheral Arteries, Brit. J. Surg. **24:** 350-361 (Oct.) 1936; Embolectomy in the Treatment of Circulatory Disturbances of the Extremities, Surg., Gynec. & Obst. **36:** 309-316 (March) 1923.

3. Lewis, Thomas: Pain as an Early Symptom of Arterial Embolism and Its Causation, Clin. Sc. **2:** 237-251 (July) 1936.

4. Scupham, G. W., and de Takats, Geza: Peripheral Vascular Disease: A Review of Some of the Recent Literature and a Critical Review of the Surgical Treatment, Arch. Int. Med. **60:** 522-563 (Sept.) 1937.

provoking recurrence of the occlusion after embolectomy has been performed. Arterial thrombosis usually originates on a background of peripheral arteriosclerosis and myocardial disease. There is frequently a previous history of intermittent claudication, coldness and discoloration of the extremities. Injury to the vessel intima as a result of arteriosclerosis and slowing of the circulation from myocardial disease with insufficiency are the important inciting factors in arterial thrombosis. The relationship of this condition to anticoagulant therapy will be discussed later in the paper.

Localization of the site of embolic occlusion does not usually present any great difficulty. The best clinical guide to the site of occlusion is the first bifurcation of the main arteries above the upper limit of physical findings (i. e., numbness, coldness, discoloration and the like). Thus, for example, in the lower extremity, if the upper limit of physical findings is at the knee joint, the probable site of occlusion is the bifurcation of the common femoral artery. The explanation for the difference between the anatomic site of the occlusion and the level of physical findings is that the collateral circulation is usually well able to supply nutrient blood for a considerable distance beyond the site of occlusion, until, that is, occlusion of the collaterals also occurs as a late thrombotic process. Visualization of the site of block by means of arteriography has also been utilized but is frequently not practicable and usually not necessary.

TREATMENT

The prime requisite to proper therapy in acute arterial embolism of the extremities is a constant awareness of the possibility of such an accident by those treating patients with heart disease, thereby enabling prompt, early recognition of the condition. Every hour lost before treatment is instituted threatens not only the life of the limb but the life of the patient as well. The immediate measures to be taken in every early case are threefold: (1) relief of arterial spasm, (2) slowing of the blood clotting time to minimize intravascular thrombosis and (3) prompt operative embolectomy if a trial of conservative medical therapy has not restored the circulation.

Relief of arterial spasm can be effected by two measures: (1) the use of papaverine hydrochloride intravenously and (2) interruption of the sympathetic pathways by paravertebral block. The intense arterial spasm is believed to be responsible for the resulting pain and for the closure of collateral vessel openings distal to this site of occlusion. It is best combated by intravenous papaverine hydrochloride, in ½ to 1 grain (0.03 to 0.06 Gm.) doses, to be repeated at intervals of one hour. In a small percentage of cases papaverine has undoubtedly caused a sufficient release of spasm to permit the passage of the embolus beyond a major arterial bifurcation, permitting restoration of circulation by this conservative measure. However, McKechnie and Allen [5] believe that, if there is not a prompt restoration of circulation after the first or second intravenous dose of papaverine hydrochloride, further conservative therapy is useless and immediate operative embolectomy should be performed. My associates and I have continued the administration of papaverine hydrochloride postoperatively to control pain and combat any vascular spasm resulting from operative trauma. Graham [6] advises the use of papaverine hydrochloride and other nonoperative measures, such as passive vascular exercise, only for cases seen too late for operative embolectomy. Griffiths [7] reports poor results with papaverine hydrochloride and conservative measures such as pavaex therapy, stating that such procedures merely caused prolonged delay and prevent early operative intervention. Denk,[8] on the other hand, is confident that he has obtained satisfactory results in a fair number of cases by the intensive use of papaverine hydrochloride alone.

Linton [9] states that the early use of paravertebral block to interrupt sympathetic pathways and counteract arterial spasm is useful in preventing blockage of collaterals and in controlling pain. Roome [10] also reports the use of lumbar sympathetic block for the relief of pain and spasm following acute arterial occlusion but states that in his experience it has had no effect on the subsequent development of gangrene if embolectomy is not performed. Leriche [11] advises arteriectomy, that is, actual excision of the portion of the artery containing the clot, under the following conditions: (1) if operation is performed more than twenty-four hours after embolic occlusion, (2) if the endothelium under the embolus appears severely damaged and (3) if gangrene threatens despite embolectomy. He believes that this procedure abolishes reflex spasm above and below the site of obstruction.

It is our belief that conservative measures may be tried for four to six hours after occurrence of the embolic occlusion, and if after this time such measures have not caused prompt restoration of circulation immediate operative embolectomy should be performed. Or if six to ten hours have already elapsed since the onset of the occlusion, operative embolectomy should be performed without further delay.

TECHNIC OF OPERATION

The site of the operative approach is anesthetized with local infiltration of procaine hydrochloride. In all 4 cases here reported operation was performed at the site of the common femoral artery, a vertical incision extending from Poupart's ligament along the course of the artery a distance of about 4 inches. The femoral artery is gently mobilized, after the femoral sheath has been incised, and a complete cuff of adventitia removed from the wall of the artery with the aid of saline infiltration between adventitia and muscularis. Two bulldog clamps (or rubber shod Allis clamps) are placed proximal and distal to the embolic occlusion for control of arterial hemorrhage. With the clamps in place (under the specific control of an assistant), an incision is made axially through the vessel wall distal to the embolus. The organized embolic mass is identified and dislodgment is gently attempted by catheter suction or an

5. McKechnie, R. E., and Allen, E. R.: Sudden Occlusion of the Arteries of the Extremities: Study of One Hundred Cases of Embolism and Thrombosis, Surg., Gynec. & Obst. **63**: 231-240 (Aug.) 1936.

6. Graham, Duncan: Embolism and Thrombosis of the Larger Arteries: Their Diagnosis and Treatment, Canad. M. A. J. **36**: 33-38 (Jan.) 1937.

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9. Linton, R. R.: Peripheral Arterial Embolism: A Discussion of the Postembolic Vascular Changes and Their Relation to the Restoration of Circulation in Peripheral Embolism, New England J. Med. **224**: 189-194 (Jan. 30) 1941.

10. Roome, N. W.: Sympathetic Blockade in Peripheral Vascular Accidents, Canad. M. A. J. **44**: 594-596 (June) 1941.

11. Leriche, René; Fontaine, René, and Dupertuis, S. M.: Arterectomy in the Treatment of Occiusive Arterial Disease, Surg., Gynec. & Obst. **64**: 149-155 (Feb.) 1937.

intra-arterial scoop. The proximal bulldog or rubber shod Allis clamp is then opened in situ by the assistant and the intra-arterial blood pressure will usually force the embolic mass out through the arterial incision. If the embolus has been driven out in one piece, there will immediately follow a forceful stream of blood under full arterial pressure, and the assistant is instructed to close the proximal clamp. If such a forceful arterial gush does not result, the artery must be carefully investigated further proximally to dislodge one or more additional embolic masses higher up, possibly in the region of the external iliac. Such intra-arterial probing must be done extremely gently, with as little trauma to the intima as possible. When a forceful arterial flow has been obtained, the proximal clamp is replaced and the distal clamp is opened. If no blood flow results from the distal vessel, it is probably occluded by a propagation thrombus, which must be carefully dislodged by catheter suction or careful, gentle intra-arterial manipulation. The degree of organization, its extent and adherence to the vessel intima will depend on the length of time elapsed between the onset of the occlusion and the operation. In 1 of our cases, the distal propagation thrombus removed in one piece measured 14 inches. When full arterial flow has been reestablished from both proximal and distal openings of the artery, closure of the axial incision in the artery is performed by a careful, continuous eversion suture of fine black silk affecting approximation of the intima in eversion. Whenever necessary, several interrupted sutures are taken to control bleeding from the incision in the artery when the clamps are removed. As soon as closure of the arterial wall is completed, a full arterial pulsation can be seen transmitted down along the distal vessel, and in some cases there is immediate restoration of warmth, color and peripheral pulsation in the lower limb.

The basis for the use of heparin in thrombosis and embolism has been thoroughly established by Murray [12] and Best in intensive studies. We have essentially followed their technic of administration, as follows: The heparin solution is added to an intravenous saline drip. Usually 1,000 units of heparin, i. e., 10 mg., is added to each hundred cubic centimeters of saline solution. The saline and heparin mixture is allowed to run into the vein at such a rate that the clotting time of the patient's blood is maintained at about fifteen minutes, i. e., two or three times the normal value. The rate at which the solution runs in is usually about 25 drops a minute but may vary from case to case. The clotting time may be determined by one of the simple methods, such as the breaking off of bits of a capillary tube filled with blood obtained by superficial capillary bleeding. In cases in which there is associated heart failure when administration of large amounts of intravenous fluids was contraindicated, McClure and Lam have used the injection of undiluted heparin, repeated every three hours, with satisfactory maintenance of the clotting time at about fifteen minutes, that is, using about 100 mg. every three hours. By the continuous intravenous drip method, about 20 to 25 mg. an hour is sufficient to maintain the clotting time at the desired level. We have used the intermittent administration of undiluted heparin as required by the cardiac status of the patient, with satisfactory results. The need for an antiheparin is rather unimportant, since the clotting time returns to normal within one hour after its administration has been stopped. We have made it a practice to begin the administration of heparin as soon as the diagnosis of an embolic arterial occlusion is made, and it is continued whenever feasible for ten days, by which time it is felt that adequate reestablishment of circulation has taken place. The preoperative administration of heparin makes for rather a bloody field at the operative site but has in no way interfered with hemostasis or healing of the operative wound.

All instruments and suture materials are kept immersed in sterile liquid petrolatum, and the operative field is kept constantly flushed with a warm 2 per cent solution of sodium citrate. Very fine black silk on an atraumatic eye needle is used for arterial suturing and hemostasis. When the operative procedure is completed, the limb is carefully wrapped in thick cotton batting, reinforced with flannel bandage, from the toes to the groin. Postoperatively, general body warmth is maintained, and heparin and papaverine hydrochloride administration are continued for five to ten days, depending on the rapidity with which a satisfactory clinical result is obtained.

PROGNOSIS

Most authors are in agreement that a living limb one month after embolectomy may be considered a successful result. Key,[2] in a study of a series of 382 cases in Sweden, states that prognosis depends on the following factors: 1. The mortality rate of limb and patient rises rapidly after six hours following the occurrence of the acute embolic occlusion. 2. The poor general condition of patients subject to embolic occlusions militates against successful results. 3. Previous arteriosclerosis and rough handling of the vessel involved during operation predisposes to postoperative thrombosis involving collateral vessels as well as the main vessel.

Of this series of 382 cases, Key reports that in 22 per cent the operation was successful, in 18 per cent subsequent amputation was required, and in 60 per cent the patient died in the hospital within one month after the operation. Of sixty-six embolectomies performed on the iliac vessels, only ten were successful.

Griffiths states that the numerous failures after embolectomy are due to prolonged delay, late recognition of the condition and time consuming attempts at conservative therapy after operative treatment has been instituted. Danzis, in a review of case reports from the literature, found that there were 60 per cent successful results among those patients operated on within the first four hours and only 18 per cent successful results among those operated on after twelve hours. Of those patients not receiving embolectomy, 13 per cent had amputations and 87 per cent were dead within two weeks after the acute embolic occlusion. The latest operation with a successful result was that of Holst, in which a femoral embolectomy was done twenty-seven hours after occlusion.

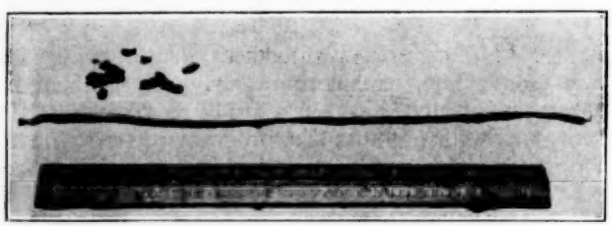
Graham offers the following as the causes of failure of restoration of circulation to the limb after embolectomy: (*a*) recurrent embolic accidents, (*b*) preexisting organic disease of the peripheral arteries and (*c*) reformation of the thrombus on the damaged intima.

12. Murray, G. D. W.: Heparin in Surgical Treatment of Blood Vessels, Arch. Surg. **40**: 307-325 (Feb.) 1940; Heparin in Thrombosis and Embolism, Brit. J. Surg. **27**: 567-598 (Jan.) 1940.

Lund,[13] in another review of a large group of cases in Sweden, states that the patients who did not have an embolectomy nearly all died within a short period of time whether they had gangrene and amputation or not. Of those patients successfully operated on, 25 per cent were dead in one year, 50 per cent in three years, 66 per cent in five years and 85 per cent in ten years.

REPORT OF CASES

CASE 1.—H. B., a white man aged 49, admitted to the medical service of the Metropolitan Hospital on April 22, 1941, complained chiefly of difficulty in breathing and swelling of the scrotum and ankles of one year's duration, which had become progressively worse; he had previously been hospitalized elsewhere for the same complaints. Significant physical findings at the time of admission were auricular fibrillation, systolic murmur at the cardiac apex, a blood pressure of 130/80, moist rales at both lung bases, liver enlarged 5 cm. and tender to palpation, questionable presence of ascitic fluid and 4 plus edema of the ankle. An electrocardiogram indicated auricular fibrillation, severe myocardial damage, suggestive coronary artery disease, possibly rheumatic. Therapy consisted of mercupurin, digitalis, theophylline with ethylenediamine; clinical improvement was good until May 15, when the patient experienced a sudden severe pain in the left foot with a feeling of coldness and numbness in the left leg and thigh. Examination about one hour after the onset revealed cyanosis, coldness and



Specimens removed at operation in case 3: above, multiple, hard, organized, embolic masses removed through opening in common femoral artery; below, single, distal, tail-like propagation thrombus 14 inches in length removed retrograde through opening in common femoral artery.

diminished sensation of the left leg up to the knee. All peripheral pulses were absent, with the exception of the femoral, which was poorly palpable. Oscillometric readings were completely absent below the groin. Operation was performed four and one-half hours after the embolic accident, through a longitudinal incision in the upper part of the left thigh under local anesthesia. The common femoral artery was exposed and incised longitudinally. An embolic mass about ½ inch in diameter was removed without resulting bleeding; a probe was inserted proximally toward the external iliac, with gradual loosening of an additional embolic mass, which was forced out of the incision in the femoral artery with a terrific gush of bleeding; this mass was about 2 inches in length, hard and well organized. Suction applied to a soft rubber catheter in the distal femoral artery removed a soft tail-like thrombus about 6 inches long. Closure of the artery and wound was performed; heparin therapy was carried out as described. Normal warmth, sensation and circulation were restored to the left leg about the fifth day after operation.

On May 27, twelve days after the embolic accident to the left leg, the patient began to complain of increasing numbness, coldness and paralysis in the right leg. These symptoms were of about eleven hours' duration before the patient thought them important enough to report to the intern. Examination revealed a mottled discoloration, coldness and diminished sensation up to about the knee. All pulses except the femoral were absent, and oscillometric readings were absent below the midthigh. Operation was performed about twelve hours after onset of symptoms, with removal from the common femoral artery of an embolic mass 1 inch in length; there was an immediate gush of blood proximally, and on removal of an 8 inch long distal propagation thrombus there was brisk bleeding from the distal femoral artery. The usual closure and postoperative therapy were carried out and satisfactory restoration of circulation to the limb was evident on the second day after operation. Of some interest are the tissue examination reports of the specimens removed at operation; the mass obtained at the first operation showed the usual firmly organized thrombus, whereas the embolus removed at the second operation revealed a decided purulent involvement of the organized clot. The patient was discharged from the hospital and has been under treatment in the cardiac outpatient department. Examination of the extremities about one year after the second embolectomy revealed both limbs to be warm and of normal sensation, with moderate edema about the ankles; the patient has had no complaints referable to the extremities.

CASE 2.—M. H., a Negro aged 26, admitted to the surgical service of the Metropolitan Hospital on April 25, 1941, complained chiefly of progressively increasing pain in the right upper quadrant of the abdomen of five days' duration. There had been no nausea or vomiting until the day of admission, when the patient vomited three times with definite aggravation of the pain in the right upper quadrant. There was no other significant past history. Physical findings at the time of admission were as follows: temperature 99.4 F., pulse rate 100 and respiratory rate 28. The abdomen was moderately distended and tympanitic, with exquisite tenderness, muscle resistance and hyperesthesia in the right upper quadrant. There was a sinus tachycardia with reduplication of the second sound; the blood pressure was 142/100, the white blood cell count 14,600 with polymorphonuclear leukocytes 88 per cent; urinalysis was negative except for a faint trace of albumin. The admission diagnosis was acute cholecystitis. The patient was treated expectantly for three days, and with no evidence of clinical improvement and a rising white blood count cell laparotomy was performed. The gallbladder and ducts were entirely normal, and no other intra-abdominal disorder was found except slight enlargement and hyperemia of the liver. Postoperatively the patient continued to have a spiking temperature with persistent tachycardia and increasing dyspnea; on repeated occasions he had episodes of severe pain in the left lower quadrant, the right lower quadrant and the left kidney region. An electrocardiogram showed auricular changes and myocardial damage. Blood cultures were repeatedly negative and urines showed granular casts. The Wassermann reaction was reported 3 plus. On May 29 (approximately one month after the onset of illness) the patient complained of coldness and loss of feeling and power in the right lower extremity. Examination revealed all pulses absent below the femoral artery, coldness, impaired sensation and absence of oscillometric readings below the right groin. A diagnosis was made of embolic occlusion of the right common femoral artery and operation was performed fourteen hours after the first onset of leg symptoms. An embolic mass about ¾ inch in diameter was removed from the common femoral artery and a long tail-like thrombus 8 inches in length was removed from the distal femoral artery with full restoration of femoral bleeding. The usual operative and postoperative technic was followed. On the third day after operation the right lower extremity was warm and had regained normal sensation; the peripheral pulses were still not obtainable. The medical condition persisted unchanged, and medical consultation was of the opinion that the entire clinical picture could be explained on the basis of an active myocarditis with mural thrombi and repeated visceral and peripheral embolic episodes.

CASE 3.—F. K., a white woman aged 64, admitted to the Flower and Fifth Avenue Hospitals on Sept. 29, 1941, had been under treatment for the past year for auricular fibrillation with mild cardiac decompensation. During the previous three weeks she had complained of precordial pain, palpitation and dyspnea. About twelve hours prior to admission the patient complained of severe pain in the calf of the right leg followed by a sensation of weakness and numbness in the leg. She massaged the leg and applied a hot water bottle to the calf region before calling her family physician, who made a diagnosis of embolic occlusion. Repeated intravenous papaverine hydrochloride was unsuccessful and operative intervention was advised. At the

13. Lund C. C.: The Treatment of Embolism of the Greater Arteries, Ann. Surg. **106:** 880-909 (Nov.) 1937.

time of admission to the hospital about twelve hours after the occurrence of the accident, the right leg was cold and cyanotic with patchy mottling up the knee, almost completely insensitive and showing evidence of a second degree burn of the calf region. Oscillometric readings were not obtained below the groin. The heart was enlarged to the left and downward, with clinical evidence of auricular fibrillation, an enlarged tender liver and a moderate amount of pulmonary basal rales. The blood pressure was 128/80. Operation was performed about thirteen hours after onset by the usual technic; it was noted on the operating table that the femoral pulse, which had previously been palpable, could no longer be obtained. When the common femoral artery was opened there was no bleeding. By combined careful probing and catheter suction several hard organized embolic masses were expelled from the opening in the femoral artery, followed by a powerful gush of bleeding. There was no bleeding from the distal femoral artery; catheter suction was applied and a single tail-like propagation thrombus about 14 inches in length was removed, followed by free active bleeding from the distal femoral. Almost immediately after repair of the arterial wound the foot and leg were warm to palpation and peripheral pulses were felt. Postoperative convalescence was entirely normal except for separation of the burned skin from the calf and great toe; excellent vascular granulations and filling in took place in a comparatively short time. At the last follow-up examination nine months after operation the patient was up and about, moderately active and under good cardiac regulation; she had, however, developed a progressive psychosis, apparently on a cerebrovascular basis.

SUMMARY

1. A survey of the recent literature emphasizes that prompt operative intervention (within six to eight hours after acute embolic occlusion) offers a good prognosis for a live limb and a live patient.

2. Of those patients not receiving the benefit of embolectomy, about 90 per cent die within two weeks, whether amputation is performed or not.

3. Patients under treatment for chronic cardiovascular disease should be constantly observed for the possibility of an acute embolic occlusion of the extremities.

4. Arterial embolectomy of the extremities is a simple, safe operative procedure performed under local anesthesia, with no mortality rate per se.

5. The introduction of heparin therapy has remarkably facilitated the surgery of embolism and has minimized the danger of recurrent thrombosis.

6. The attempts at conservative treatment of acute embolic occlusion should not be prolonged beyond six hours after occurrence of the accident; if these measures are unsuccessful after a six hour trial, immediate surgery should be performed.

7. Of the four successful embolectomies reported two were performed on 1 patient for two separate embolic accidents. The number of hours elapsed between the onset of embolic arterial occlusion and the time of operation were respectively four and one-half hours, twelve hours, fourteen hours and thirteen hours.

Intuition in Science.—We often underrate the importance of intuition. In almost every scientific problem which I have succeeded in solving, even those that have involved days or months of work, the final solution has come to my mind in a fraction of a second by a process which is not consciously one of reasoning. Such intuitive ideas are often wrong. The good must be weeded out from the bad—sometimes by common sense or judgment—at other times by reasoning.—Langmuir, Irving: Science, Common Sense and Decency, *Science* **97**:1 (Jan. 1) 1943.

USE OF PENICILLIN IN SULFONAMIDE RESISTANT GONORRHEAL INFECTIONS

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The preparation of a highly concentrated and active form of penicillin was first reported by Chain, Florey and others [1] in 1940. In 1941 Abraham and others [2] reported more extensively on their investigative studies including the first clinical trials. They mentioned that the growth of six different strains of Neisseria gonorrheae was inhibited in dilutions in the order of 1 : 2,000,000. Another strain was inhibited only up to 1 : 32,000. These investigators, however, pointed out that the actual figures reported must be taken with reserve because the potency of the penicillin varied as the work progressed. If the end point was based on twenty-four hour readings, the results may indeed vary considerably. Subsequent experience largely has confirmed this early work.[3] Herein we report experimental and clinical results with Neisseria gonorrheae. While we have prepared small amounts of penicillin, the material used in our studies was furnished for the most part through the courtesy of Abbott Laboratories, Incorporated.

Because of the limited amounts of penicillin available, it did not seem justifiable to use penicillin in gonorrheal infections which are fairly amenable to sulfonamide therapy. The need, however, is apparent for an effective therapeutic agent against infections due to this organism which are known to be resistant to sulfonamide preparations. We elected, therefore, to study the effect of penicillin experimentally against several strains of Neisseria gonorrheae isolated from patients in treatment of whom adequate sulfonamide therapy had failed.

EXPERIMENTAL DATA

In vitro tests to determine the bactericidal action of penicillin on Neisseria gonorrheae were done in the following manner on three strains of the organism: A laked blood base was used for the test because by previous experience it had been found the most satisfactory method for preserving the viability of Neisseria gonorrheae. It was made by adding to sterile distilled water an equal amount of sterile citrated blood. Two different lots of penicillin were used, the first of which contained 174 Oxford units per milligram and the second 230 Oxford units per milligram. A primary dilution of 1 : 500 was made of the first lot and a com-

From the Division of Medicine (Dr. Herrell), the Section on Urology (Dr. Cook) and the Section on Bacteriology (Dr. Thompson), the Mayo Clinic.

1. Chain, E.; Florey, H. W.; Gardner, A. D.; Heatley, N. G.; Jennings, M. A.; Orr-Ewing, J., and Sanders, A. G.: Penicillin as a Chemotherapeutic Agent, Lancet **2**: 226-228 (Aug. 24) 1940.

2. Abraham, E. P.; Chain, E.; Fletcher, C. M.; Gardner, A. D.; Heatley, N. G.; Jennings, M. A., and Florey, H. W.: Further Observations on Penicillin, Lancet **2**: 177-188 (Aug. 16) 1941.

3. Heilman, Dorothy H., and Herrell, W. E.: Comparative Antibacterial Activity of Penicillin and Gramicidin: Tissue Culture Studies, Proc. Staff Meet., Mayo Clin. **17**: 321-327 (May 27) 1942. Herrell, W. E., and Heilman, Dorothy: Tissue Culture Studies on Cytotoxicity of Bactericidal Agents: I. Effect of Gramicidin, Tyrocidine and Penicillin on Cultures of Mammalian Lymph Node, Am. J. M. Sc. **205**: 157-162 (Feb.) 1943. Herrell, W. E.; Heilman, Dorothy H., and Williams, H. L.: The Clinical Use of Penicillin, Proc. Staff Meet., Mayo Clin. **17**: 609-616 (Dec. 30) 1942. Hobby, Gladys, L.; Meyer, Karl, and Chaffee, Eleanor: Activity of Penicillin in Vitro, Proc. Soc. Exper. Biol. & Med. **50**: 277-280 (June) 1942; Observations on the Mechanism of Action of Penicillin, ibid. **50**: 281-285 (June) 1942; Chemotherapeutic Activity of Penicillin, ibid. **50**: 285-288 (June) 1942. Meyer, Karl; Chaffee, Eleanor; Hobby, Gladys L.; Dawson, M. H.; Schwenk, Erwin, and Fleischer, G.: On Penicillin, Science **96**: 20-21 (July 3) 1942. Herrell.[4]

parable dilution in terms of Oxford units was made of the second lot, which was also considered to be 1 : 500 for the purpose of this experiment. These primary dilutions then were used to make the higher dilutions of penicillin in the laked blood base. Preliminary trials showed that dilutions of 1 : 100,000 and 1 : 200,000 were most suitable for the tests, since the end point in the test could be reached before there was any great

TABLE 1.—*The Antibacterial Effect of Penicillin on Neisseria Gonorrheae*

Strain	Dilution	1 Hr.	2 Hrs.	3 Hrs.	4 Hrs.
1	1:100,000	+++	0	0	0
	1:200,000	+++	+	0	0
	Control	+++	+++	+++	++
2	1:100,000	+++	+++	+	0
	1:200,000	+++	+++	+	0
	Control	+++	+++	+++	++
3	1:100,000	+++	++	+	0
	1:200,000	+++	++	+	0
	Control	+++	+++	+++	++

+++, heavy growth; ++, moderate growth; +, slight growth; 0, no growth.

reduction of numbers of the bacteria in the control tubes. A heavy suspension of Neisseria gonorrheae was made in 1 cc. of the laked blood base by removing the growth from the surface of a chocolate blood agar plate which had been incubated from twenty-two to twenty-four hours. Enough of this heavy suspension was added to the dilutions of penicillin in laked blood and to the control tube of laked blood so that if a 3 mm. loopful was streaked at once on a chocolate blood agar plate the resulting culture would show between 300 and 400 colonies. The tubes were placed in an incubator at 37 C. and subcultures were made on chocolate blood agar at hourly intervals from the test dilutions and from the control tube.

The results obtained are shown in table 1. It was noted that there was a sharp drop in the number of viable organisms in contact with penicillin between the first and the second hour in strains 1 and 3 and between the second and the third hour in strain 2. Table 1 also shows that all the organisms in contact with the dilutions of penicillin were no longer viable after three or four hours, while the control tubes still had large numbers of viable organisms. It was apparent that after four hours there was some reduction of the number of organisms in the control tubes, and for that reason it was thought best to use such dilutions of penicillin as would give an end point within that period.

CLINICAL TRIALS

Penicillin, in addition to being antibacterial for the organism, fortunately is excreted rather rapidly in the urine. The twenty-four hour urine of patients receiving the amounts of penicillin used will usually contain approximately 3 Oxford units of penicillin per cubic centimeter of urine. In other words, between a third and a half of the material is excreted through the urinary apparatus. This is, of course, highly desirable in the treatment of infections of the type being considered. The high degree of solubility of the material also permits it to reach the involved tissues readily. From these observations, therefore, it seemed entirely logical to expect satisfactory clinical results from the use of penicillin in the treatment of infections due to Neisseria gonorrheae.

In view of the highly effective antibacterial activity of penicillin against these strains of Neisseria gonorrheae, the 3 patients from whom they were isolated were treated with the intravenous administration of penicillin according to the method recently described by one of us.[4] For the treatment of these infections the largest amount of penicillin administered in twenty-four hours was 32,000 Oxford units. Half of the twenty-four hour dose was dissolved in 1 liter of isotonic solution of sodium chloride. If for any reason the administration of isotonic solution of sodium chloride is undesirable, penicillin may be administered in a 5 per cent solution of dextrose in triple distilled water without any loss of activity. Initially between 100 and 200 cc. of the material is administered intravenously at a fairly rapid rate. Following this the rate of injection is regulated to between 30 and 40 drops per minute. The second liter containing penicillin may be attached to the continuous intravenous system eight to ten hours later. Repeated venipunctures may be avoided by allowing the solution of dextrose to drip in slowly during the interval in which penicillin is not being administered. A simple arm splint is applied to keep the arm in position. This is tolerated well by the patient and renders the continuous intravenous administration possible and not uncomfortable. When pyrogen free penicillin has been used, no toxic reactions have been observed. The solution containing penicillin is made up immediately before use. There is no evidence of loss of potency of the material which is kept in the closed system and is administered in the manner described. It should not be overlooked that administration of the solution of penicillin is continuous rather than intermittent.

A summary of the amounts of penicillin used, the number of days of administration and the results in the 3 cases herein reported is shown in table 2.[5] The rather striking and early clinical improvement together with the complete lack of any toxic effect due to administration of penicillin was gratifying.

CASE 1.—A white man aged 30 presented himself because of a urethral discharge which had persisted for thirty days. The urethritis had its onset six days after exposure. He was treated immediately with an adequate course of sulfathiazole but nothing more than temporary improvement was obtained. He received another course of sulfathiazole as an ambulatory patient without any apparent effect. He then was hospitalized for a third attempt at chemotherapy.

TABLE 2.—*Penicillin Therapy in Sulfonamide Resistant Gonorrhea*

Case	Smear	Chocolate Blood Agar Culture	Penicillin: Total, Mg.	Penicillin: Oxford Units	Days Treated	First Negative Culture, Hrs.	Result
1	Positive	Positive	340	68,000	2½	17	Cure
2	.....	Positive	391	92,000	3½	48	Cure
3	Positive	Positive	442	104,000	3½	48	Cure

At the time of his admission a complete general examination gave negative results. There was a copious urethral discharge which on smear and culture showed the presence of Neisseria gonorrheae. The genitalia were normal otherwise. The prostate was slightly enlarged and tender. The complete blood examination, including a flocculation test for syphilis, gave entirely normal results. The routine examination of urine revealed a slight amount of albumin, and the microscopic examination showed an occasional erythrocyte and pyuria, grade 4 on the basis of 1 to 4.

4. Herrell, W. E.: Further Observations on the Clinical Use of Penicillin, Proc. Staff Meet., Mayo Clin. **18:** 65-76 (March 10) 1943.

5. Since this paper was submitted for publication we have used penicillin in 2 additional cases of sulfonamide resistant gonorrhea. In 1 case, in which the infection had been present for four months, the cultures became negative forty-eight hours after the administration of penicillin was started. In the other case the infection had been present for eleven months and the first negative culture was obtained in twenty-one hours.

The patient was hospitalized and penicillin therapy was begun. Penicillin was administered by the intravenous drip method. The first liter contained 16,000 Oxford units and its administration was started at 5 p. m. on the day of his admission. Five hours after the treatment was begun the patient stated that the dysuria and urethral distress had subsided completely. By 10 a. m. the following day there was no urethral discharge, and no material could be obtained even after prostatic massage. In other words, the patient was free from symptoms within seventeen hours after the institution of penicillin therapy. Prostatic secretion and first urine cultures taken seventeen hours after the institution of treatment did not reveal any Neisseria gonorrheae. Another attempt at culture was made twenty-four hours later but the results were completely negative. Forty hours after the institution of treatment routine urinalysis did not reveal any albumin, and the microscopic examination revealed no erythrocytes and only an occasional pus cell.

During the first twenty-four hours the patient received 2 liters of the penicillin preparation, which represented a total of 32,000 Oxford units, or 160 mg. For the second twenty-four hours he received 2 liters of the penicillin preparation, each containing 12,000 Oxford units, or a total of 24,000 units for the second twenty-four hours. He received 1 more liter of penicillin after this which contained 12,000 Oxford units, and because of the complete absence of any clinical findings treatment was discontinued and he was dismissed. Ten days later the patient returned for examination. He had been completely well and cultures taken after he had imbibed alcohol rather heavily and following coitus were entirely negative. The patient has remained entirely free from symptoms.

CASE 2.—A white man aged 29 had been ill for five weeks. He had had a persistent purulent urethral discharge due to a gonorrheal infection contracted following exposure shortly before his illness. He had received sulfathiazole, sulfanilamide and finally sulfadiazine in amounts which would be considered quite adequate. Six days before admission there had developed acute urinary retention which required catheterization for relief. At that time purulent urine was obtained. Severe bilateral pain in the lower part of the abdomen had developed with some extension into both flanks. The patient suffered a great deal of pain during the act of urination and there were extreme frequency and urgency. His temperature ranged between 99 and 101 F. The prostate was enlarged, grade 4. It was extremely tender and the possibility of a prostatic abscess was considered. Examination of the abdomen revealed extreme tenderness and muscular spasm in both lower quadrants. There was also some tenderness in both lumbar areas. The temperature on admission was 101 F. The remainder of the physical examination gave negative results.

The routine urinalysis did not reveal any albumin or sugar. Microscopic examination revealed occasional erythrocytes and pyuria grade 2, with 50 cells per field. The concentration of hemoglobin and the erythrocyte count were normal. However, the leukocyte count was 14,600 per cubic millimeter of blood and the sedimentation rate was 94 mm. per hour. Cultures of the prostatic secretion and first urine revealed many gonorrheal organisms present.

Penicillin therapy was begun shortly after the laboratory studies were reported. During the first twenty-four hours the patient received 32,000 Oxford units of penicillin given as previously described. During the second twenty-four hours he received 24,000 Oxford units. During the third twenty-four hours another 24,000 Oxford units was administered, and during the final twelve hours of treatment 12,000 Oxford units, the total duration of treatment being three and a half days. Five and a half hours after the institution of treatment the patient stated that the abdominal pain and soreness, which had been very distressing, had subsided completely. He continued to have some perineal distress and the prostate was quite tender on examination. Forty-eight hours after the institution of treatment the prostate was less tender and it was approximately half the size it had been previously. The patient had little difficulty in urinating and stated that he felt entirely normal. His temperature did not rise above normal after the first twenty-four hours of treatment. When forty-eight hours of treatment had been completed, cultures of the urine following prostatic massage did not reveal any gonorrheal organisms. Two subsequent cultures were also entirely negative. The patient was allowed to be up and around the hospital but did not receive any more therapy after treatment for three and a half days. Two days later he was dismissed. He was fr[illegible] from symptoms and the final culture of the prostatic urine after massage was negative. The routine urinalysis gave completely negative results except for the presence of four pus cells per field.

CASE 3.—A youth aged 18 was admitted with a complaint of a urethral discharge which had persisted for four months. The urethritis had developed two days after exposure, and treatment had been instituted immediately following the diagnosis of gonorrheal urethritis. The first course of treatment consisted of sulfathiazole for twelve days. His dysuria and urethral pain were relieved but the discharge continued. Subsequent to this he had a course of twelve days' treatment with sulfanilamide. There was no diminution of the urethral discharge, and bacterial cultures remained positive. A third course, which consisted of sulfanilamide, then was given. Following this he was treated for two and a half months by means of sulfathiazole given in courses with short rest periods. There was no improvement. Finally he received local urethral instillations of mild protein silver.

At the time of admission there was much urethral discharge. The prostate was slightly enlarged and quite tender. The remainder of his physical examination gave essentially negative results. The routine urinalysis showed albuminuria grade 2. The microscopic examination revealed occasional erythrocytes and pyuria grade 4. The concentration of hemoglobin was normal and the flocculation reaction for syphilis was negative. The leukocyte count was 9,600 per cubic millimeter of blood. Smears of the urethral discharge and chocolate blood agar cultures were both positive for Neisseria gonorrheae.

Penicillin therapy was instituted as soon as the diagnosis of gonorrheal urethritis and prostatitis was confirmed. During the first and second days of treatment the patient received 32,000 Oxford units of penicillin per day. The third day he received 28,000 Oxford units, and during the first twelve hours of the fourth day he received 1 liter containing 12,000 units. Twelve hours after the initiation of treatment the patient stated that the dysuria associated with urination was practically gone. At this time there was still a slight amount of urethral discharge. However, the patient stated that it was less than he had noted for one month. Except for a slight urethral discharge he felt practically normal by the end of forty-eight hours' treatment. At this time bacterial cultures of the prostatic secretion and first urine were entirely negative. Another similar specimen obtained twenty-four hours later did not reveal any Neisseria gonorrheae. The microscopic examination of the urine revealed between 20 and 30 cells per microscopic field. The patient was dismissed. A recheck examination seven days later did not reveal any evidence of gonorrheal infection, and bacterial studies again gave entirely negative results.

SUMMARY

We have studied experimentally the antibacterial activity of penicillin against several strains of Neisseria gonorrheae isolated from patients in whom the infection was completely resistant to what might be considered adequate treatment with sulfonamide preparations. These strains of organisms are inhibited completely in fairly high dilutions of an active form of penicillin. Bacterial cultures reveal that the number of organisms is decreased greatly at the end of one or two hours' contact with penicillin. Between the second and third or third and fourth hours in contact with penicillin no viable organisms were found. This experimental evidence immediately suggests that penicillin should prove effective in the treatment of clinical infections due to these sulfonamide resistant bacteria.

The complete absence of toxicity following the intravenous administration of pyrogen free penicillin, the lack of any discomfort to the patient and the rather rapid disappearance of clinical symptoms have been observed in three cases of sulfonamide resistant gonor-

rheal infections. Because of the limited amounts of penicillin available, we feel that penicillin therapy should be reserved and studied further in those cases in which the infection is resistant to the accepted forms of treatment now being used. In all the cases reported, in addition to the clinical response noted, negative bacterial cultures were obtained sometime between seventeen and forty-eight hours after the institution of pencillin therapy.

EXTRAPULMONARY KLEBSIELLA PNEUMONIAE INFECTIONS

AN ANALYSIS OF THE LITERATURE: REPORT OF TWO UNUSUAL CASES WITH RECOVERY

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In 1882 Friedländer [1] announced the discovery of a micro-organism which he believed to be the cause of lobar pneumonia and which, in his original communications, he described as a micrococcus. Since this time many reports of infection due to Klebsiella pneumoniae (commonly called Friedländer bacillus) have appeared in the literature, especially during the past twenty-five years. A review of these papers, as well as of the popular textbooks of today, makes it evident that most of the attention has been focused on the pulmonary lesions with their complications. The literature dealing with extrapulmonary Klebsiella pneumoniae infections is scanty and has not been correlated. This has prompted the writing of this paper along with a desire to report 2 unusual cases with recovery and the use of sulfadiazine therapy in 1.

BACTERIOLOGY

Morphology.—During the first few years following the discovery of the organism there was much confusion, owing to a superficial resemblance between Friedländer's organism and Diplococcus pneumoniae.[2] However, in 1886 Fränkel [3] and Weichselbaum,[4] by their careful researches, were able to show that the "micrococcus" of Friedländer was really a short encapsulated bacillus. Since this time enough data have been accumulated so that the morphologic characteristics can be agreed on. Klebsiella pneumoniae is a short, gram negative, plump rod with rounded ends and is surrounded by a large capsule. The organisms are often relatively small and arranged in pairs. The average measurements are from 0.5 to 1.0 micron in width and 1 to 3 microns in length. Forms approaching both extremes may be encountered in one and the same culture. On prolonged cultivation they may become pleomorphic and grow out as long rods or filamentous or even club shaped bacilli. They are nonmotile and possess no flagella. Spores are not formed. The bacillus is characteristically surrounded by a well developed capsule, which is most perfectly demonstrated in preparations taken directly from some animal fluid, such as the secretion or exudate from infected areas.

Physiology.—The organism is easily cultivated, growing readily on all the usual culture mediums. Growth is most rapid at a temperature of 37.5 C. but occurs also between 12 and 45 C. It is aerobic and facultatively anaerobic. The growth on agar is very characteristic, appearing glossy, smooth and viscid. The colonies are large, grayish white and extremely mucoid. From the papers of Osterman and Rettger [5] one finds that the Klebsiella pneumoniae group is an extremely variable one and is most apt to be confused with the coli-aerogenes group. These authors have done considerable work in the differentiation of these groups.

Classification.—Klebsiella pneumoniae is known by many names. Various authors have referred to the organism as the Friedländer bacillus, Bacillus pneumoniae, Bacillus mucosus capsulatus, Pneumobacillus and Bacillus encapsulatus pneumoniae. Julianelle in 1926 [6] and again in 1930,[7] by the study of agglutination and precipitin reactions, was able to distinguish three types, A, B and C. All others were placed in a heterogeneous group X. It is quite probable that in the future group X may be further broken down, just as was group IV of the pneumococcus. Klebsiella pneumoniae A is by far the most frequently seen; B is immunologically related to the pneumococcus type II; the C group appears infrequently and is much less virulent than the first two.

Distribution.—Ford [8] states that Klebsiella pneumoniae is widely distributed in nature, as it has been shown to exist in the soil, in the air, in dust, in mud and in canal water.[9] It also appears to be a rather frequent inhabitant of the human body both in the respiratory and in the intestinal tract. Bloomfield [10] reports that 5.8 per cent of normal persons have the bacillus present in the respiratory tract—most frequently localized in and about the tonsils. Dudgeon [11] states that the organism is found in the intestinal tract of 5.5 per cent of normal persons.

Primary Sites of Infection in One Hundred and Ninety-Eight Cases

Primary Site	Number	Per Cent
Gastrointestinal tract	61	31
Genitourinary tract	50	25
Biliary passages and liver	46	23
Lungs and upper respiratory tract	25	12.5
Miscellaneous skin and meninges	10	5
Vagina, uterus and adnexa	6	3.5

SITE OF PRIMARY INFECTION

Although in the minds of most physicians and in textbooks the organism is primarily associated with pneumonia or other infections of the respiratory tract, Baehr, Shwartzman and Greenspan,[12] in a report of 198 cases from the Mount Sinai Hospital in New York, claim that this conception is wrong. They make the statement that the respiratory tract is a less common site of primary infection. The primary sites found in the 198 cases reported by them are given in the accompanying table.

From the Surgical Service of Grace Hospital.

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3. Fränkel, Albert: Ztschr. f. klin. Med. **10**: 426, 1885-1886.
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5. Osterman, E., and Rettger, L. F.: A Comparative Study of Organisms of Friedländer and Coli-Aerogenes Groups, J. Bact. **42**: 699-719, 721-743 (Dec.) 1941.
6. Julianelle, L. A.: A Biological Classification of Encapsulatus Pneumoniae, J. Exper. Med. **44**: 113 (July), 683 (Nov.), 735 (Dec.) 1926.
7. Julianelle, L. A.: The Distribution of Friedländer Bacilli of Different Types, J. Exper. Med. **52**: 539 (Oct.) 1930.
8. Ford, W. W.: Textbook of Bacteriology, Philadelphia, W. B. Saunders Company, 1927, p. 562.
9. Gay, F. R., and his associates: Agents of Disease and Host Resistance, Springfield, Ill., Charles C Thomas, Publisher, 1935, p. 691.
10. Bloomfield, A. L.: The Mechanism of the Bacillus Carrier with Special Reference to the Friedländer Bacillus, Am. Rev. Tuberc. **4**: 847 (Jan.) 1921.
11. Dudgeon, L. S.: A Study of Intestinal Flora Under Normal and Abnormal Conditions, J. Hyg. **25**: 119 (July) 1926.
12. Baehr, George: Shwartzman, Gregory, and Greenspan, E. B.: Bacillus Friedländer Infections, Ann. Int. Med. **10**: 1788-1801 (June) 1937.

From the table one may readily see that the intraperitoneal combination of gastrointestinal and biliary tracts account for more than 50 per cent of the cases. The lungs and upper respiratory tract, including the pharynx, tonsils, larynx and nose, in this series of cases, appear as the primary sites in only 12.5 per cent.

PREDISPOSING CAUSES

Listed in various textbooks and papers, the main predisposing causes are alcoholism, trauma and submergence. In reviewing the latest cases, diabetes mellitus appears to be a common accompanying condition. What role the diabetes plays is hard to say—it may tend only to lower the patient's resistance and so make him more susceptible to Klebsiella pneumoniae infections as well as to other infections. Baehr and his associates [12] point out that stasis in the biliary or urinary tract, either by stone, neoplasm or external pressure, definitely plays a role in predisposing to infection in these regions.

PATHOLOGIC AND CLINICAL FEATURES

The pathologic lesions vary with the site of primary infection and the subsequent course of events. In the experimental work reported by Gay and his associates [9] subcutaneous inoculation in mice produced a spreading lesion containing a viscid exudate consisting of fibrin, bacilli and leukocytes. Intraperitoneal injection into mice resulted in death. Autopsy revealed viscid stringy exudate containing leukocytes in the peritoneal cavity, general septicemia being demonstrated by cultures.

In the human being the pathologic condition produced in the lungs has been well described. The pathologic condition is not as well known in the extrapulmonary lesions. However, from the reported cases, one can see that Klebsiella pneumoniae is a pathogen which may be associated with suppurative processes in any part of the body, more particularly in the gastrointestinal, genitourinary and biliary systems. The suppurative processes tend to be extensive and of a rapidly spreading nature. In many cases complications such as septicemia, liver abscesses, meningitis, pelvic abscesses and subphrenic abscesses make their appearance.

Intra-abdominal infections are usually secondary to a perforative lesion of the colon or appendix. Eighty-seven per cent of the cases reported by Baehr and his associates [12] resulted from appendical abscesses. Other causes may be perforation of a carcinoma, rupture of a diverticulum or traumatic perforation of the bowel. In these cases peritonitis occurs and may be rapidly followed by subphrenic abscess, liver abscesses, empyema, septicemia and pulmonary metastatic abscesses.

Primary liver abscesses, fortunately, are uncommon. Boettiger and his associates,[13] who reported 2 cases resulting in death, say that in their review of the literature less that 25 cases of primary liver abscesses have been reported since 1900. Many of these cases, reported as primary liver abscesses, are probably in reality secondary to intestinal or biliary disease, for, like Escherichia coli and other intestinal organisms, Klebsiella pneumoniae may enter the portal system and be excreted by the liver. Under this circumstance excretory infections are apt to occur if stasis is present.

In the urinary tract Klebsiella pneumoniae is often associated with other organisms—Escherichia coli, Proteus vulgaris and Bacillus pyocyaneus most commonly. Here again when stasis is present, excretion of the organism through the kidney is apt to cause infection. During the past few years in American journals prostatic [14] and perirenal [15] abscesses with complicating pathologic conditions have been reported.

Baehr and his associates [12] in their series found that 38 of the 46 patients with infections of the biliary tract had gallstones in the gallbladder or common bile duct. The pus in the infected gallbladder and common duct tends to be thin and presents no distinctive features, although in some cases it may be foul smelling, thick and mucoid.

In the female genital tract suppuration is present—usually in the adnexa. Pelvic abscesses are apt to develop. A case of uterine gangrene and septicemia following criminal abortion was reported by Hipp in 1936.[16]

In the ears a purulent otitis media occurs and is apt to be followed by mastoiditis. Cavernous sinus phlebitis has also been reported.[17]

Cases of primary meningitis, osteomyelitis and keratitis have been recorded both in American and in foreign journals.

As a caustive agent in septicemia Klebsiella pneumoniae is rather uncommon, for Kolmer,[18] in his observations on 282 cases of septicemia of all types, remarks that Klebsiella pneumoniae septicemia is rarely encountered. However, when Klebsiella pneumoniae infection does already exist, septicemia is not too unusual. Baehr and his associates [12] report that in 16 of their 198 cases (8 per cent) septicemia developed. Meyer and Amtman [19] in 1939 brought out the fact that 109 cases of Klebsiella pneumoniae septicemia had been reported in the literature. Since 1939 a few more cases have been added to the literature. A feature of interest is that in many of the cases of septicemia the site of origin remained obscure. However, with the newer knowledge that in about 75 to 80 per cent of cases the primary site of infection is in the gastrointestinal, genitourinary or biliary tract, it is quite probable that the original focus will be discovered more often.

COURSE

The course of Klebsiella pneumoniae infections depends on the location of the primary site and the complicating features. In general the disease usually starts rather suddenly with fever and malaise; local pain and tenderness are present. As the infection progresses, the suppurative process soon becomes evident with the cultures showing the organism in large numbers. Until recently a fulminating course with many complicating features has been the usual accepted picture. Of late it has been recognized that Klebsiella pneumoniae infections may also run a chronic low grade course in extrapulmonary lesions as well as in pulmonary infections, as reported by Solomon.[20]

13. Boettiger, Carl; Weinstein, Mandel, and Werne, Jacob: Primary Suppuration of Liver Due to Friedländer's Bacillus, J. A. M. A. **114:** 1050-1055 (March 23) 1940.

14. Pfeiffer, D. B.: Klebsiella Pneumoniae Bacteremia Due to Prostatic Abscess: Case with Recovery, Ann. Surg. **106:** 1115-1118 (Dec.) 1937.

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16. Hipp, J.: Uterine Gangrene and Septicemia Due to Friedländer Bacillus Following Criminal Abortion: Case, Ann. d'anat. path. **13:** 116-121 (Jan.) 1936.

17. Allen, B.: Otitis Cavernous Sinus Phlebitis Due to Friedländer Bacillus, J. Mount Sinai Hosp. **2:** 169-173 (Nov.-Dec.) 1935.

18. Kolmer, J. A.: Ann. Int. Med. **8:** 612-631 (Nov.) 1934.

19. Meyer, K. A., and Amtman, Leo: Treatment of Friedländer's Septicemia by Sulfapyridine with Recovery, J. A. M. A. **113:** 1641-1642 (Oct. 28) 1939.

20. Solomon, Saul: Chronic Friedländer Infections of Lungs: Report of Seventeen Cases and Observations on Therapy with Sulfapyridine and Sulfanilamide, J. A. M. A. **115:** 1527-1536 (Nov. 2) 1940.

TREATMENT AND PROGNOSIS

During the early history of Klebsiella pneumoniae infections the only treatment given was supportive and symptomatic. As a result the prognosis was uniformly grave. Although definite mortality figures for extrapulmonary lesions are not available during this early period, in a review of the literature from 1882 to 1938 of pulmonary lesions Hartman [21] found 232 cases with satisfactory records of Klebsiella pneumoniae pneumonia with a mortality of 94 per cent. In the 198 cases reported by Baehr and his associates [12] in 1937 biliary tract infection carried a mortality of 30 per cent as compared with 17 per cent mortality in urinary tract infections. In this report also 16 cases of Klebsiella pneumoniae septicemia occurred, of which 4 were not fatal (a mortality rate of 75 per cent).

Another nonspecific form of treatment instituted shortly after the turn of the century was surgical drainage. There is no doubt that this procedure in many cases did save lives.

During the past few years, besides the use of several chemical agents, including the iodides, more specific therapy in the form of serum and the sulfonamide compounds has been introduced.

According to Robertson,[22] type II antipneumococcus serum, which is known to cross agglutinate certain members of the Friedländer group, has been used with some success. Perlman and Bullowa [23] agree that this serum may be of value in Klebsiella pneumoniae B infections.

An autovaccine has been used with successful results, as reported in some of the foreign journals.[24]

Bullowa,[25] using specific serum therapy in 8 cases of Klebsiella pneumoniae pneumonia, reports a mortality of 50 per cent as compared with a mortality of 89 per cent in the non-serum treated group. The use of serum is still in the experimental stage and, although theoretically it may sound good, it is not very practical, for the serum is not easily available, the cost is high and the cases for treatment are so few that the serum degenerates between infrequent usage.

The sulfonamide compounds, more particularly sulfapyridine, have given some hopeful results. Long and Bliss [26] in their book report favorably both from experimental and from clinical studies. Solomon [20] was encouraged by the results with sulfapyridine in his series of 17 cases of chronic pulmonary infections. Cures have been reported in various journals since 1939 with sulfonamide therapy in the treatment of Klebsiella pneumoniae septicemia,[27] meningitis [28] and pneumonia.[29]

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24. Rouffart-Marin, J.: Septicemia Due to Friedländer Pneumobacillus; Case Cured by Autovaccine, Bruxelles méd. **19:** 1145-1146 (July 16) 1939. Fingerland, A.; Hub, M., and Maršálak, J.: Chronic Suppurative Diseases of Adnexa Due to Friedländer Pneumobacillus Successfully Cured with Autovaccine, Časop. lék. česk. **78:** 1145-1147 (Oct. 20) 1939.
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26. Long, P. H., and Bliss, Eleanor A.: The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds, New York, Macmillan Company, 1939, p. 36.
27. Dérot, M., and Dutrey, M.: Septicemia Due to Friedländer Bacillus with Pulmonary Localization: Cure After Sulfapyridine Therapy: Case, Bull. et mém. Soc. méd. d. hôp. de Paris, **56:** 541-544 (Oct. 29) 1940.
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29. Muschenheim, C.: Chronic Friedländer Infections of the Lung, Internat. Clin. **3:** 216-224 (Sept.) 1940. Sinclair, F.: Friedländer Pneumonia Successfully Treated with Sulfapyridine, Brit. M. J. **1:** 196 (Feb. 8) 1941.

REPORT OF CASES

CASE 1.—*History.*—W. R., a white man aged 52, a machine operator, admitted to Grace Hospital in 1941, had one week previously suddenly become aware of a sharp aching pain on the inner aspect of his left ankle. The pain was continuous, radiated upward toward the knee and persisted to the time of admission. Swelling and redness appeared about the inner aspect of the ankle after three days and then rapidly increased. He became bedridden at this time because of pain and the increasing swelling and soreness. There was no history of any injury to the ankle or any part of his body. He had had no previous similar episodes. He stated that he had not had a recent cold or sore throat and he had no urinary or gastrointestinal complaints.

He had been known to have diabetes for one year before admission to the hospital, controlled on a diabetic diet and 20 units of insulin daily. A careful review of the systems revealed no abnormalities. There had been no previous operations or accidents. He had been drinking alcoholic beverages in moderation. He had been married for thirty-three years and his wife and six children were alive and well.

Physical Examination.—The patient was alert and cooperative and complained of pain in the left ankle. The ears, nose, mouth and throat were normal except for extremely carious teeth. The heart, lungs and abdomen were normal. A rectal examination revealed the prostate to be slightly enlarged but not tender, irregular or boggy. Local examination of the left ankle revealed tenderness, swelling and redness of the ankle and foot. Motion of the ankle was limited almost completely because of pain. No external abrasion or laceration could be seen. There was no evidence of lymphangitis or lymphadenitis. His temperature was 101.4 F., pulse rate 94, respiratory rate 20 and blood pressure 120 systolic and 70 diastolic.

Laboratory Examinations.—Examination of the urine at the time of admission revealed 4 plus sugar and 2 plus acetone; blood sugar was 350 and nonprotein nitrogen 40. White blood cells numbered 28,000 with 90 per cent polymorphonuclear leukocytes, of which 12 per cent were nonsegmented. The red blood cell count was 4,800,000 and the hemoglobin content 92 per cent (Dare method). The Wassermann and Kahn reactions of the blood were negative.

Course.—The diabetic service was called in to treat the patient's diabetic condition. Treatment in the form of elevation of the extremity, ice bags to the foot and ankle later changed to hot magnesium sulfate soaks, sedation and sulfathiazole 2 Gm. immediately and 1 Gm. every four hours was instituted.

During the first week in the hospital the patient appeared quite toxic; his temperature ranged between 101 and 104 F. A blood culture yielded no growth. X-ray examinations revealed no evidence of osteomyelitis of the ankle. The sulfathiazole blood level remained between 4 and 5 mg. per hundred cubic centimeters. Sedimentation time was fifteen minutes, and the repeated white blood cell count was 22,000 with 78 per cent polymorphonuclear leukocytes. The foot and ankle became more swollen and then localized abscesses appeared over the lateral and medial malleoli and over the dorsum of the ankle. On the eighth hospital day he was taken to the operating room, where the abscesses were incised and drained, with the release of large quantities of chocolate colored viscid pus. Cultures of this pus yielded a pure growth of Klebsiella pneumoniae classified as belonging to group A.

Repeated blood cultures were negative. Smears and cultures from the nose and throat were negative for Klebsiella pneumoniae. During the next few days there was a rapid progression of the suppurative process up the leg, with many areas of fluctuation appearing in the leg. The patient was given a transfusion of 650 cc. of citrated blood and again was taken to the operating room, where multiple incisions were made in the leg. Pus was found extending throughout the entire leg, subcutaneously, in the fascial spaces and in the muscle bellies. Because of this, most of the leg was laid open and rubber catheters were inserted through and through for drainage and irrigation. He was given another transfusion postoperatively and was placed on sulfadiazine therapy with an initial dose of 4 Gm. and then 1 Gm. every four hours. The pus again yielded Klebsiella pneumoniae in pure culture. Repeated

blood cultures again were negative and repeated x-ray examinations of the left ankle were negative for osteomyelitis. Irrigation of the leg with 5 per cent solution of sodium sulfadiazine was carried out through the catheters. During the next week (third week) the patient looked and felt much improved; his temperature returned to between 99 and 100.4 F. and the white blood cell count diminished. However, on the eighth day following these last incisions it was noticed that the leg was again filling up with purulent material, his temperature rose to 101 F. and his white blood cell count rose to 27,500 with 90 per cent polymorphonuclear leukocytes.

A midthigh amputation was decided on in an attempt to save the patient's life. This was done under spinal anesthesia. During the amputation a pocket of pus was encountered on the lateral aspect of the thigh. This region was gently but carefully debrided, sulfadiazine 5 Gm. was inserted locally and the stump was left open except for one suture to bring the skin over the end of the bone. Cultures of the pus from this region again showed the Friedländer organism. He was again placed on sulfadiazine postoperatively and was given two transfusions of 300 cc. each. During the next twelve days he appeared to be making good progress, the stump remained fairly clean, no new progression of the infection was noticed and his temperature remained normal. The sulfadiazine level remained between 5 and 7 mg. per hundred cubic centimeters. The stump granulated in well and the remainder of his course was uneventful except for the necessity of having a small abscess opened up at the midportion of the stump, which soon healed over. He was discharged on crutches on his forty-eighth hospital day, twenty-eight days after the midthigh amputation.

Second Admission.—Approximately two months after discharge from the hospital the patient was readmitted with pain, tenderness and swelling of the stump and with a temperature of 103 F. Soon after this admission the stump opened spontaneously and discharged about 200 cc. of foul smelling, chocolate colored pus; cultures of this showed Klebsiella pneumoniae. After observation for six days, during which time the stump did not seem to drain well, he was taken to the operating room, where the draining abscess of the stump was opened up widely and all the infected granulation tissue was carefully scraped out. Sulfadiazine 10 Gm. was inserted locally and he was started on the same drug 1 Gm. every four hours by mouth. The blood concentration of the drug was maintained between 6.5 and 9 mg. per hundred cubic centimeters for the next two weeks and then gradually decreased. He remained afebrile, the stump healed well and his diabetes was easily controlled. Four weeks after this second admission he was discharged to his family physician. He was seen in the surgical follow-up clinic two weeks, two months and four months after discharge. At each return visit he showed more improvement; he was gaining weight and the stump remained well healed. He was seen again one year after onset of his infection, at which time he was wearing a permanent type of prosthesis and was walking about with the aid of a cane. He had gained 35 pounds (16 Kg.), his general health was excellent and the stump was clean and well healed.

CASE 2.[30]—M. M., a housewife aged 39, admitted to Grace Hospital in October 1937, had a typical history and physical manifestations of an acute exacerbation of chronic cholecystitis with cholelithiasis. All other systems were normal. A Graham visualization test of the gallbladder revealed a pathologic nonfilling gallbladder but no definite evidence of gallstones. On the sixth hospital day she was taken to the operating room, where a gangrenous gallbladder containing stones was removed. The gallbladder was so friable that during its removal it was torn open. A cigaret drain was inserted in the operative region before the abdominal wall was closed. The patient felt well during the first twenty-four hours but then had respiratory distress and cyanosis and a spiking temperature course began, 100 to 104 F. Physical examination and x-ray examinations with a portable apparatus were suggestive of either atelectasis or pneumonitis in the right lower lobe. During the next three weeks she had a stormy septic course during which time the operative wound stopped draining; repeated white blood cell counts ranged between 18,000 and 35,000 with polymorphonuclear leukocytes between 80 and 90 per cent. Two blood cultures were negative. She was given repeated transfusions, parenteral fluids and oxygen intermittently as needed. A subphrenic abscess was suspected during the latter part of this three week period and finally it was deemed advisable to explore the subphrenic region. A thoracotomy was done in the eighth interspace in the posterior axillary line. Considerable serosanguineous fluid was found in the pleural cavity, the wound was packed with dry gauze and on aspiration with a needle through the diaphragm dirty yellowish green viscid pus was aspirated. This pus yielded a pure culture of Klebsiella pneumoniae. The patient was placed on sulfanilamide therapy, and several days later the subphrenic region was entered from above and a mushroom catheter was inserted through the diaphragm. Drainage was profuse for the first two days, consisting of fibrin, leukocytes and red blood cells. Cultures of the drainage were positive for the gram negative Friedländer organism. Later on the amount of drainage decreased and cultures showed Klebsiella pneumoniae and Bacillus pyocyaneus. During the next three weeks the patient was kept on a regimen of sulfanilamide medication and repeated small transfusions. She improved slowly both clinically and by x-ray evidence and was discharged from the hospital eight weeks from the date of admission. At home the thoracotomy wound drained for about five weeks and then closed spontaneously. X-ray films at this time showed decided improvement; the diaphragm was elevated and the pleura was thickened, but there was no evidence of fluid levels of any pocketing abscess. She has been followed at intervals during the past five years. After an initial period of two years, during which time she complained of weakness, easy fatigability, an occasional cough and aches and pains in the joints of her shoulders and hands, she has been feeling well, complaining only of mild dyspnea on moderate exertion for the past three years.

30. Reported through the courtesy of Dr. Anthony J. Mendillo.

COMMENT

Both of the cases herein reported are examples of extrapulmonary Klebsiella pneumoniae infections. The first case apparently was one of infection in the soft tissues about the ankle as the primary site of the infection, although there was no local trauma and there were no abrasions or lacerations. Cultures of material from the nose and throat were negative for Klebsiella pneumoniae, as were several blood cultures. Stool cultures were not done, but the patient exhibited no symptoms or signs of enteritis or colitis. The organism was definitely established by the various differential tests as Klebsiella pneumoniae belonging to group A. The suddenness of onset was typical, as were the suppurative process and the septic course. As in many of the latest cases reported, the man had diabetes mellitus as an accompanying condition. When an abscess was encountered during the midthight amputation, it was felt that the patient's prognosis was poor, for the infection was a severe progressive one with a very virulent strain of Klebsiella pneumoniae, as evidenced by the previous rapid extension throughout all the tissues of the leg. I have little doubt that adequate surgical drainage and the use of sulfadiazine, both locally and generally, brought about recovery in this case. Septicemia did not occur or else was so transitory that it was not picked up in the repeated blood cultures.

Case 2 is similar to cases reported by Baehr and his associates in that the primary site of the Friedländer infection was in the biliary tract. As is usual in many of these cases there was a "parade" of complicating pathologic conditions. In this case a localized peritonitis was followed by a subphrenic abscess and then later by empyema. The predisposing cause here was probably stasis in the biliary tract due to stones. Here again recovery was probably brought about by the combination of adequate surgical drainage and sulfanilamide therapy.

SUMMARY AND CONCLUSIONS

1. In 2 unusual cases of extrapulmonary Klebsiella pneumoniae infections recovery occurred.

2. The use of sulfadiazine in case 1 is, I believe, the first recorded instance of the use of this drug for Friedländer infections in the literature.

3. The combination of adequate surgical drainage, when possible, and sulfonamide therapy at present appears to be the best form of treatment.

4. Because of a persistent high mortality rate in Klebsiella pneumoniae infections it is felt that further therapeutic trials should be attempted with the newer sulfonamide compounds and also with the newer antibacterial agents such as gramicidin, penicillin and aspergillin.

Clinical Notes, Suggestions and New Instruments

THROMBOPENIC PURPURA DEVELOPING AS A COMPLICATION OF SULFATHIAZOLE AND SULFADIAZINE THERAPY

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Although many types of complications have been described since the sulfonamide compounds were introduced into the treatment of infectious diseases, there are not many instances in which thrombopenia with associated purpura has been reported as a complication of therapy with these drugs. Markel and Rike [1] reported the development of hematuria, melena and oozing of blood from the gums and a wound incision in a case in which sulfanilamide was given postoperatively. The platelet count was 180,000, the bleeding time was "prolonged" and the clotting time was normal, but the clot failed to retract in twelve hours. Necropsy failed to demonstrate any abnormality of the bone marrow. Hoffman [2] reported hematuria, gingival bleeding, a hemorrhagic macular rash covering the lower extremities and melena in a case in which sulfapyridine was given. No blood studies were reported. Baradulin [3] described a generalized purpuric rash with multiple petechiae in the mucous membranes of a patient who received "streptocidin" (a sulfonamide compound). The tourniquet test was positive, but further studies were not reported. Dolgopol and Hobart [4] reported a diminution of platelets in association with a severe leukopenia in a case in which sulfapyridine was given. Goldbloom and his associates [5] described a toxic thrombopenia in a woman aged 50 who received 90 grains (6 Gm.) of sulfapyridine. The platelet count dropped to 25,000 and the bleeding time was prolonged to twenty-five minutes, with a delayed clot retraction time. Gingival hemorrhages and vaginal bleeding developed. Bone marrow studies were negative. The platelets were suppressed for three days and then returned to normal. Kracke [6] mentioned a case in which severe thrombopenia was presumptively due to the administration of sulfathiazole. Quick and Lord [7] described the findings in a case of acute hemolytic anemia which developed after the administration of sulfathiazole. The patient had a purpuric rash and a positive reaction to the tourniquet test. Mention was not made of the number of platelets in the blood. Rosenfeld and Feldman [8] reported the occurrence of a severe thrombopenic hemorrhagic state during the administration of sulfathiazole. During the thrombopenic reaction, the platelet count was 2,000 per cubic millimeter, the bleeding time was six minutes, the coagulation time was four minutes and the tourniquet test was strongly positive. Five days after discontinuance of sulfathiazole, the platelets were again abundant and subsequent doses of sulfathiazole failed to produce the thrombopenic state. Werner [9] reported a case of thrombopenic purpura which was due to idiosyncrasy to sulfathiazole. The patient was given 13.9 Gm. of sulfathiazole over a period of five days, at which time a slight rash developed. Twenty days later he was given 1 Gm. of the drug and purpuric signs developed within twelve hours. Platelets were not present in the blood smear. Finally, Meyer and Perlmutter [10] reported the findings in a case of aplastic anemia secondary to sulfathiazole. At the height of the reaction, the patient had no platelets in the blood smear, 1,710,000 red blood cells per cubic millimeter, 5 Gm. of hemoglobin per hundred cubic centimeters of blood and 1,600 white blood cells per cubic millimeter with only 8 per cent of neutrophils.

We wish to report 2 cases in which thrombopenia developed after the administration of the sulfonamide compounds. In the first case thrombopenia developed after the administration of sulfathiazole and on subsequent testing the same manner of reaction was found to sulfadiazine. In the second case purpura developed during the administration of sulfadiazine, and death occurred.

CASE REPORTS

CASE 1.—J. H., a married man aged 61, a clothes cutter, was admitted to the Rochester Municipal Hospital Nov. 9, 1941, with a history of sudden onset twenty-four hours previously of shaking chills, weakness, fever and pain in the lower left part of the chest aggravated by breathing and coughing. Twelve hours before admission his cough was productive of bloody sputum. On examination the temperature was 39.5 C. (103.1 F.) rectally, pulse rate 110, respiratory rate 28 and the blood pressure 100 mm. of mercury systolic and 66 mm. diastolic. He was dyspneic and acutely ill. He complained bitterly of pain in the left lower part of the chest. The cough was still productive of bloody sputum. Physical signs of consolidation were present in the left lower lobe of the lungs. The remainder of the examination was not remarkable. There were no purpuric lesions.

The laboratory data were as follows: The blood Wassermann reaction was negative. The red blood cell count was 5,600,000 per cubic millimeter. The blood hemoglobin was 14.5 Gm. per hundred cubic centimeters and the white blood cell count was 19,000 per cubic millimeter. The blood smear showed 94 per cent neutrophils and a normal number of platelets. Urinalysis was negative. A roentgenogram of the chest demonstrated consolidation in the left lower lobe. Blood and sputum cultures were positive for type II pneumococcus.

Sulfathiazole was given by mouth in divided doses. After 12 Gm. had been given an oozing epistaxis was noted. At this time the nonprotein nitrogen value of the blood was 50 mg. per hundred cubic centimeters and the total protein value of the blood 5.4 Gm., the albumin being 3 Gm. and the globulin 2.4 Gm. The blood sulfathiazole level was 4.8 Gm. The mild epistaxis persisted and for the first time a petechial rash appeared over the legs and buttocks and in the oral mucous membranes. Two frankly bloody stools were passed. Administration of sulfathiazole was immediately stopped after

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a total of 14 Gm. had been given in a period of thirty-six hours. At this time the Francis test was negative, the blood leukocytes numbered 12,700 per cubic millimeter and the hemoglobin was 10.2 Gm. per hundred cubic centimeters. The blood smear showed 90 per cent neutrophils and 10 per cent lymphocytes. Only 1 platelet was seen in the entire preparation. Examination of the urine revealed no abnormalities. The blood nonprotein nitrogen value was decreased to 35 mg. per hundred cubic centimeters and the sulfathiazole level was 5.5 mg. Six hundred cc. of compatible fresh citrated whole blood and 160,000 units of type specific antipneumococcus rabbit serum were administered promptly. There was rapid clinical improvement and the platelets reappeared in the blood smear. All purpuric tendencies ceased. Serum sickness developed fourteen days after the administration of rabbit serum.

When the patient had completely recovered from the serum reaction and the pneumonia it was thought advisable to test him for sensitivity to sulfathiazole. The patient showed no reaction to the scratch test, the patch test and the intradermal injection of a 10 per cent saline suspension of the drug. Following this, 0.1 Gm. and 0.25 Gm. were given orally on successive occasions and no fall in the platelet count was observed. At this time three doses of 1.5 Gm. of sulfathiazole were administered by mouth at four hour intervals. Eight hours after this test had been started there was a definite diminution of the platelets in the peripheral blood smear. The bleeding time was increased to eight minutes and the Rumpel-Leede test became positive. A tendency to spontaneous bleeding was not noted.

The patient left the hospital and returned two weeks later, Jan. 5, 1942, for a careful evaluation of his sensitivity to sulfathiazole and sulfadiazine. The observations made at this time appear in table 1.

TABLE 1.—*Results of Experiments Made in Case 1*

Date	Time	Drug, Gm.	White Blood Cells per Cu. Mm.	Red Blood Cells, Millions per Cu. Mm.	Platelets Estimated from Smear	Platelets per Cu. Mm.	Bleeding Time in Minutes	Rumpel-Leede Test	Clotting Time in Minutes	Differential Blood Smear P	L	M	E	B
					Sulfathiazole Experiment									
1/ 5/42	1 p. m.	1.5	7,900	3.87	Adequate	190,000	3.5	Negative	7, 7, 10	75	15	8	1	1
	5 p. m.	1.5	.....	3.75	Decreased	75,000	3.5	5 petech.						
	9 p. m.	1.5	.....	....	Decreased	35,000	7.0	40 petech.	.....	73	21	4	1	1
1/ 6/42	1 a. m.	...	.....	....	Rare	40,000	7.0	40 petech.						
	9 a. m.	...	.....	....	.....	55,000								
	12 n.	...	.....	....	.....	.....	...	.....	5, 9, 9					
	5 p. m.	...	.....	....	.....	80,000	3.0							
1/ 7/42	9 a. m.	...	.....	....	Decreased	75,000	...	.....	.....	73	13	9	2	3
	4 p. m.	...	.....	3.79	.....	100,000	...	6 petech.						
1/ 8/42	9 a. m.	...	8,800	....	Decreased	90,000	...	.....	.....	68	23	7	1	1
	4 p. m.	...	.....	....	.....	115,000								
1/ 9/42	9 a. m.	...	.....	....	Adequate	95,000	...	Negative	.....	63	28	8	1	0
	4 p. m.	...	.....	....	.....	120,000	...	Negative						
1/10/42	9 a. m.	...	.....	....	Adequate	130,000	...	Negative	.....	65	28	7	0	0
1/12/42	9 a. m.	...	.....	....	Adequate	170,000	...	Negative	.....	76	15	8	1	0
					Sulfadiazine Experiment									
1/12/42	9 a. m.	...	.....	....	Adequate	170,000	...	Negative	.....	76	15	8	1	0
	1 p. m.	2.0	.....	....	Adequate	170,000	3.5	Negative	9, 5, 7					
	5 p. m.	2.0	.....	....	.....	110,000	...	Negative						
	9 p. m.	1.0	.....	....	.....	75,000	4.0	14 petech.						
1/13/42	1 a. m.	1.0	.....	3.70	Decreased	70,000	4.0	8 petech.						
	9 a. m.	2.0	.....	3.65	.....	90,000	...	6 petech.						
	4 p. m.	...	.....	3.60	Very rare	45,000	4.0	12 petech.	.....	65	26	7	2	0
1/14/42	9 a. m.	...	6,600	3.69	Decreased	85,000	...	.....	.....	73	22	3	1	1
	4 p. m.	...	.....	....	.....	115,000	...	Negative						
1/16/42	8 p. m.	...	.....	....	Adequate	120,000	3.0	Negative	.....	66	23	8	1	2
1/19/42	8 p. m.	...	.....	....	Adequate	140,000	3.0	Negative	.....	75	14	6	2	3

Clotting time was done by the Lee-White method.
Rumpel-Leede test was done by reading the number of petechiae in 1 square inch area of the skin after a cuff was applied to the arm for 5 minutes with the pressure kept midway between the systolic and diastolic levels.
P refers to neutrophils, L to lymphocytes, M to monocyes, E to eosinophils and B to basophils. The figures indicate the percentage of each of these cells.
On all clotting times reported in this table, the clot retraction was good.

CASE 2.—C. B., a widow aged 79, was admitted to the Rochester Municipal Hospital on Feb. 26, 1942 with a history of onset of chills and fever one week previously. Three days before admission to the hospital a cough productive of blood streaked sputum developed and fever as high as 102 to 103 F. per cubic millimeter, and the blood smear showed 86 per cent neutrophils and adequate platelets. The red blood cells were normal. Type VIII pneumococcus was isolated from the sputum. A blood culture was negative. A roentgenogram of the chest showed consolidation in the right upper and right lower lobes.

Shortly after admission, 140 cc. (approximately 318,000 units) of type VIII antipneumococcus rabbit serum was administered without a reaction. Sulfadiazine was given by mouth in amounts sufficient to maintain a blood level between 9 and 13 mg. per hundred cubic centimeters. On February 27 six more vials (approximately 150,000 units) of rabbit serum was given intravenously. The patient continued to appear acutely ill, with persistent signs of consolidation and increased respirations. On March 2 it seemed apparent that congestive heart failure was developing and rapid digitalization was undertaken. Throughout this period the white blood cells remained elevated between 13,000 and 19,000 per cubic millimeter, and the temperature ranged between 38 and 39.5 C. (100.4 and 103.1 F.). Repeated blood cultures, examination of the urine and repeated

roentgen examinations of the chest failed to reveal any cause for the unfavorable clinical course. The sputum was retyped and again found to contain type VIII pneumococcus. A thoracentesis was performed on March 6. Twenty cc. of blood tinged, sterile fluid was obtained. Throughout this period, the patient received 3 Gm. of sulfadiazine each day without manifesting any toxic symptoms. A few crystals were noted in the urine, but the urinary output and sediment and the blood nonprotein nitrogen remained within normal limits.

On March 8, the patient suddenly had a precipitous drop in the white blood cell count from 26,000 to 4,900 per cubic millimeter. The following day a generalized hemorrhagic and petechial rash was noted. This was most prominent over the chest, in the axillas, over the lower part of the abdomen and over the posterior wall of the chest. Small petechiae were noted in the conjunctivas and mucous membranes of the mouth. There was no melena or hematuria. The Rumpel-Leede test was strongly positive. The bleeding time was three minutes and the clotting time four minutes. The clot retracted poorly and was friable. The blood smear showed a decided reduction of blood platelets. Blood studies were made daily until the patient died. Table 2 shows the pertinent findings.

Despite multiple transfusions and symptomatic treatment, the patient continued to grow weaker, with increasing manifestation of bleeding into the skin and mucous membranes, and died March 13. Permission for autopsy was not granted.

TABLE 2.—*Pertinent Findings in Case 2*

Date	Hemoglobin, Gm. per 100 Cc.	Red Blood Cells, Millions per Cu. Mm.	White Blood Cells per Cu. Mm.	Platelets Estimated from Smear	Platelets per Cu. Mm.	Blood Smear Percentage of Neutrophils
2/25/42	13.5	4.20	21,000	Adequate	.....	86
3/ 7/42	....	....	26,000			
3/ 8/42	15.5	....	4,900	.....	.....	70
3/ 9/42	....	....	15,800	Sharply reduced	.....	45
3/10/42	....	....	11,650	.....	30,000	
3/11/42	14.8	5.20	9,500	Reduced	60,000	87
3/12/42	....	....	12,650	.....	40,000	
3/13/42	....	....	.....	Reduced	30,000	85

COMMENT

The first patient had a severe thrombopenic hemorrhagic state during the administration of sulfathiazole. He received a total of 14 Gm. by mouth during a thirty-six hour period and at the same time had a severe pneumonic infection with a positive blood culture which subsequently became negative. He was also given rabbit serum and had a severe attack of serum sickness. However, when all this had cleared he was again shown to be sensitive both to sulfathiazole and to sulfadiazine, thrombopenia developing after the administration of both of these drugs. It is obvious that his sensitivity to sulfathiazole was stronger than to sulfadiazine. We did not continue our experimental dosages to the stage of spontaneous bleeding tendencies.

The second patient experienced a fatal thrombopenic hemorrhagic state during the administration of sulfadiazine. Although she had no bacteremia, it is not feasible to assume that the thrombopenia was due solely to sulfadiazine, as we cannot dismiss her general toxicity as the causative element that played a part in her fatal thrombopenic hemorrhagic state.

SUMMARY

One patient had an unequivocal sensitivity to sulfathiazole and sulfadiazine with resulting thrombopenia and purpura. The other patient experienced thrombopenia and purpura following the administration of sulfadiazine.

In view of the definite demonstration of sensitivity to the drug in case 1 two months after the first reaction to it, we feel that extreme caution should be used with reference to its readministration following the development of thrombopenia, even though Rosenfeld and Feldman [8] found that this was not true in their experience.

TOXIC REACTIONS OF PAREDRINE-SULFATHIAZOLE SUSPENSION

REPORT OF TWO CASES

MERRILL C. O'DONNELL, M.D., ST. LOUIS

As this new drug has been presented to the medical profession, it is desirable that any untoward reactions from it be brought to the immediate attention of the physician.

Paredrine-sulfathiazole suspension is a preparation introduced by the Smith, Kline and French Pharmaceutical Company. The active components are a suspension of microcrystal sulfathiazole 5 per cent in an isotonic solution of 1 per cent paredrine hydrobromide (p-hydroxy-a-methylphenethylamine). The preservative used is sodium ethyl mercuri thiosalicylate 0.005 per cent; gelatin is present in 0.1 per cent. The product has been recommended by its makers as a vasoconstrictor of the nasal mucosa, with the additional value of the antibacteriostatic action of sulfathiazole. It may be introduced into the nasal cavity and sinuses by drops, atomizer or the displacement method of Proetz. The cases under study have been treated at the Otolaryngological Clinic of the St. Louis University Group of Hospitals.

CASE 1.—C. L., a white youth aged 18, had frequently received Proetz displacements with 0.25 per cent ephedrine sulfate in isotonic solution of sodium chloride for a subacute ethmoiditis with no unfavorable reactions. When a paredrine-sulfathiazole suspension was administered in the usual manner, the immediate response of the patient was uneventful. Thirty minutes later, however, he complained of "chilly" sensations over the entire body followed by palpitations and a generalized headache. He was put to bed and given 3 grains (0.2 Gm.) of soluble pentobarbital; shortly afterward, 1 grain (0.06 Gm.) of codeine sulfate was administered hypodermically. This medication did not modify the symptoms and the headache grew more severe. Nausea, which was present throughout, terminated in severe vomiting. His temperature was subnormal (97 F.); the blood count was within normal limits. For twenty-four hours the palpitations and headache persisted to a mild degree. Forty-eight hours later, no symptoms remained and the patient had no apparent ill effects.

CASE 2.—L. V., a white married woman aged 54, had been treated for a sphenopalatine neuralgia. She had received displacement treatments three times, twice with a 0.25 per cent solution of ephedrine sulfate in isotonic solution of sodium chloride and once with the aforementioned paredrine-sulfathiazole suspension. At no time had she displayed any toxic reactions.

Twenty minutes after receiving the fourth treatment (the second with paredrine-Sulfathiazole suspension) she was seized with sudden severe pain generalized over the head. Her hands and legs had sensations of chilliness, while her heart palpitated forcibly. A few minutes later she lay down and was given 10 grains (0.65 Gm.) of acetylsalicylic acid as well as cold packs to her head; in a short while she experienced nausea, vomiting and diarrhea. The pain and discomfort increased to such an extent that, four hours after the treatment, the patient was hospitalized. Three grains (0.2 Gm.) of sodium amytal and 1 grain (0.06 Gm.) of codeine phosphate were given, resulting however in only slight alleviation of the pain. Four hours later and again in four hours, ½ grain (0.03 Gm.) of codeine was administered orally.

On admission to the hospital her temperature was 96.6 F., blood pressure 135/84, pulse rate 86 and respiratory rate 20. The blood counts were within normal limits. The headaches continued to a lesser extent into the following day, when she was able to rise from the recumbent position only with moderate to severe pain. Nausea, vomiting and diarrhea did not recur. After approximately six more hours she was completely without headaches and, although still weak, was able to continue her work.

Prior to these episodes I had not observed any reaction other than the usual headaches which occasionally accompany the Proetz displacements. The solution used was obtained from a container which had been opened several days previously but had been tightly stoppered. Other patients had similar treatments from the same solution with no complications.

1325 South Grand Boulevard.

Special Article

HANDBOOK OF NUTRITION: XXV

CONDITIONED MALNUTRITION

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The terms "malnutrition," "nutritional deficiency disease," "nutritional failure," "beriberi," "pellagra," "scurvy," "riboflavin deficiency" and similar terms signify to many persons disorders arising solely from an inadequate diet. But all these may occur in the presence of dietary adequacy. As pointed out by Kruse,[1] these terms should denote a deficiency in the bodily tissues rather than in the diet. If a tissue deficiency arises from an inadequate diet it is known as a primary deficiency. If the tissue deficiency is caused by factors other than an inadequate diet alone it is known as a conditioned or secondary deficiency. Conditioned deficiencies are caused by factors that interfere with the ingestion, absorption or utilization of essential nutrients, or by factors that increase their requirement, destruction or excretion.[2]

The importance of these conditioning factors as a cause of deficiency disease has not been generally recognized. In surveys of the nutritional status of population groups there has been a tendency to neglect the causal role of these conditioning factors and attribute all malnutrition to dietary inadequacies alone. On the other hand, in hospital and office practice the finding of clearcut gross manifestations of deficiency disease caused by conditioning factors may lead to one of the following two errors: The first is to consider the lesion a manifestation of the original or conditioning disease unrelated to tissue nutritional deficiency. The second, after recognizing the nutritional basis of the secondary manifestation, is to ascribe the original or conditioning disease to nutritional deficiency. Those making the first error ignore the existence of deficiency disease, while those making the second error attribute most deviations from normal health to malnutrition.

The prevention and treatment of these conditioned deficiency diseases are often the decisive factors in determining recovery after surgery [3] and in many severe infections. Likewise their prevention and treatment often decide the success of other therapeutic measures directed toward alleviating the conditioning disease. In addition, the comfort, length of life and economic usefulness of many patients depend on adequate nutrition.[4]

THE POSSIBLE NONSPECIFICITY OF CERTAIN LESIONS OF MALNUTRITION

The gross evidence (table 1) and the better established special examinations (table 2) for the detection of malnutrition as outlined by Jolliffe, McLester and Sherman [5] are listed in the accompanying tables. Since these manifestations, whether primary or conditioned, are identical, it is not necessary to redescribe them here. It is necessary to point out, however, that with few exceptions the findings characteristic of malnutrition are nonspecific. Some lesions attributable to malnutrition may be produced by local tissue deficiency [6] as a result of circulatory disturbances, trauma pressure or infection. These local conditioning factors may produce lesions identical with those of a systemic deficiency. Other lesions may not be related to either systemic or local tissue deficiency but may be due to some factor other than malnutrition. These facts indicate that all the diagnostic skill and clinical acumen employed by physicians in any other branch of clinical medicine must be employed in the interpretation of lesions usually ascribed to malnutrition. The following observations illustrate this point:

TABLE 1.—*Gross Evidences of Malnutrition*

System	Finding	Suggested Deficiency or Syndrome
Eyes	Xerosis conjunctivae and corneae	Vitamin A
	Central ophthalmoplegia	Thiamine
Mucous membranes	Scarlet red stomatitis and glossitis with or without secondary Vincent's infection	Nicotinic acid
	Magenta glossitis	Riboflavin
	Atrophic glossitis	Nicotinic acid, B complex, addisonian anemia, Plummer-Vincent syndrome
	Scorbutic gums	Ascorbic acid
	Cheilosis	Riboflavin
	Nonspecific urethritis, balanitis, vaginitis	Nicotinic acid
Skin	Pellagrous dermatitis	Nicotinic acid
	Seborrheic lesions in nasolabial folds on face, behind ears and in skin folds	Riboflavin
	Hyperkeratosis and hyperfolliculosis	Vitamin A
	Hemorrhagic manifestations	Vitamin K, ascorbic acid
	Fissures in angles of mouth	Riboflavin
Neurologic	Characteristic bilateral symmetrical polyneuropathy	Thiamine
	Combined system syndromes	Thiamine, B complex, addisonian anemia
	Wernicke's syndrome	Thiamine, B complex
	Nicotinic acid deficiency encephalopathy	Nicotinic acid
	Progressive stupor and hebetude	Nicotinic acid
	Certain organic reaction psychoses	Nicotinic acid, thiamine and B complex
Skeletal	Rachitic deformities and osteomalacia	Vitamin D, calcium, phosphorus
General	Underweight, underheight, edema, pallor	Calories, proteins, iron, B complex

Xerosis conjunctivae is a lesion characteristic of vitamin A deficiency in animals [7] and one that responds to massive vitamin A therapy in man.[8] From this it

1. Kruse, H. D.: A Concept of Malnutrition, Milbank Mem. Fund Quart. **20:** 245 (July) 1942.

2. Jolliffe, Norman: Chapter on Nutrition and Deficiency Diseases in Preventive Medicine in Modern Practice, New York, Paul B. Hoeber, 1942.

3. Brown, P. B., and Donald, C. J., Jr.: Prognosis of Regional Enteritis, Am. J. Digest. Dis. **9:** 87 (March) 1942. Starr, Paul: Value of Vitamins in Surgical Practice: Collective Review, Internat. Abstr. Surg. **74:** 309, in Surg., Gynec. & Obst., April 1942. Hartzell, J. B., and Crowley, R. T.: Vitamin Therapy in the Surgical Patient, Am. J. Surg. **56:** 288 (April) 1942. Pollack, Herbert; Ellenburg, Max, and Dolger, Henry: Postoperative Precipitation of Vitamin B Complex Deficiencies, J. Mount Sinai Hosp. **8:** 925 (Jan.-Feb.) 1942.

4. Jolliffe, Norman: Treatment of Neuropsychiatric Disorders with Vitamins, J. A. M. A. **117:** 1496 (Nov. 1) 1941.

5. Jolliffe, Norman; McLester, J. S., and Sherman, H. C.: The Prevalence of Malnutrition, J. A. M. A. **118:** 944 (March 21) 1942.

6. McCullough, Kendrick, and Dalldorf, Gilbert: Epithelial Metaplasia: Experimental Study, Arch. Path. **24:** 486 (Oct.) 1937. Dalldorf, Gilbert: The Pathological Responses to Vitamin Deficiencies, Bull. New York Acad. Med. **14:** 635 (Oct.) 1938. Straumfjord, J. V.: Lesions of Vitamin A Deficiency: Their Local Character and Chronicity, Northwest Med. **41:** 229 (July) 1942.

7. Bessey, O. A., and Wolbach, S. B.: Vascularity of the Cornea of the Rat in Riboflavin Deficiency, with a Note on Corneal Vascularization in Vitamin A Deficiency, J. Exper. Med. **69:** 1 (Jan.) 1939; Vitamin A, Physiology and Pathology, J. A. M. A. **110:** 2072 (June 18) 1938. Wolbach, S. W.: The Pathologic Changes Resulting from Vitamin Deficiency, ibid. **108:** 7 (Jan. 2) 1937.

8. Kruse, H. D.: Medical Evaluation of Nutritional Status: IV. The Ocular Manifestations of Avitaminosis A, with Especial Consideration of the Detection of Early Changes by Biomicroscopy, Pub. Health Rep. **56:** 1301 (July 27) 1941; Milbank Mem. Fund Quart. **19:** 207 (July) 1941.

should not be inferred that all "spots" or elevations that appear on the eyeballs peripheral to the cornea are xerosis conjunctivae. Some are, but others are pterygium and others scleral deposits of varying composition. The contention of Kruse [8] that xerosis conjunctivae is a manifestation of chronic vitamin A deficiency has been criticized by Berliner,[9] who points out that not all the photographs published by Kruse [8] were characteristic of xerosis conjunctivae, that the vitamin A blood levels are not low, and that many of the lesions in question are those usually ascribed to simple senile changes. It should be noted, however, that trained ophthalmologists after gross and slit lamp examinations frequently disagree on the appropriate anatomic labeling in a high proportion of "spot" cases. The blood level of vitamins does not necessarily reflect the state of the tissues and cannot be used as a criterion for the absence of a deficiency disease, particularly a chronic deficiency anatomically manifest.[10] In this type of malnutrition the blood reflects the recent intake of vitamin A. Also to designate lesions of the conjunctiva as senile changes with the implication that senility

TABLE 2.—*Special Examinations for Detection of Malnutrition*

Examination	Condition It May Detect
Roentgenogram of hand and wrist, elbow and hip	Rickets and scurvy in children: osteomalacia and scurvy in adults
Roentgenogram of heart	Advanced beriberi
Electrocardiogram	Changes suggestive of thiamine deficiency
Biomicroscopic eye examination with slit lamp	Capillary invasion of cornea (riboflavin deficiency); changes in conjunctivas (vitamin A deficiency)
Red blood cell count Hemoglobin Stained blood smear Red blood cell volume	Iron deficiency anemia; addisonian anemia; macrocytic anemia
Plasma ascorbic acid	Vitamin C undersaturation
Serum calcium Serum phosphatase Serum phosphorus	Vitamin D deficiency
Blood pyruvic acid	Vitamin B_1 deficiency
Serum protein or albumin	Protein deficiency
Blood prothrombin	Vitamin K deficiency

per se is responsible for them is unsatisfactory. This merely identifies the condition with a population in which it is frequently found but does not explain its cause. Even in arteriosclerosis, age is not the essential cause. As William Boyd [11] has stated, "The advance in years merely permits some slowly acting cause to produce the effects in the vessels." In discussing the lesions of chronic malnutrition, Kruse [1] states that "not all elderly persons show the changes. On the other hand they occur in children. Time, not senility, is the essential point, and time does not start the changes, it is simply a dimension over which they progress. They are specific avitaminoses in a state of chronicity, due usually to respective dietary deficiencies running over a period of years. Their prevalence and severity vary with the number and degree of deficient diets. . . . Most important of all, they are reversible, yielding slowly but completely to appropriate therapy." This latter point has been partially confirmed by Jolliffe and Stern,[12] who observed that, of 10 subjects given 50,000 units of vitamin A twice daily by mouth for ten months, 7 showed definite evidence of responding in the manner described by Kruse. It seems, therefore, that some of these lesions respond to vitamin A therapy. Some may not, but sufficient time has not yet elapsed to decide this point definitely. Complete solution of this problem requires further study, especially the biomicroscopic slit lamp examination of the conjunctivas of experimental subjects maintained with diets deficient in vitamin A.

Corneal vascularity is undoubtedly associated with riboflavin deficiency in many subjects.[13] In acute cases this condition can be observed by slit lamp biomicroscopy to disappear following riboflavin administration, to return when riboflavin is withheld and to disappear again when treatment is resumed. In this acute type of lesion the ocular symptoms of burning, itching, asthenopia, photophobia and lacrimation are extremely common. Some investigators [14] have used corneal vascularity as an index of riboflavin deficiency in surveys of population groups. Several observers [15] have warned, however, that it is not yet confirmed that all or nearly all of these vascular changes are due only to riboflavin deficiency or that they are a necessary accompaniment of other undoubted signs of riboflavin deficiency. Youmans and Patton [16] have observed a considerable number of subjects with mild but definite corneal vascularization not accompanied by ocular symptoms and in whom there was no correlation with dietary intake of riboflavin, other dietary factors or other evidence of deficiency disease. Reexamination of these subjects showed an improvement or disappearance of the vascularization in the winter or spring season compared with the fall, in spite of a lower intake of riboflavin in the former period. This study suggests that factors other than riboflavin are concerned. Youmans and Patton [16] say "there is some evidence to suggest that such a factor (there may be others) is light, . . . which may be concerned in the production of a vascularization through the mechanism of a local deficiency without any general deficiency being present. In general, the conclusion which seems indicated is that corneal vascularization, even of the characteristic type and of definite degree, does not always mean a general riboflavin deficiency." Youmans and Patton [16] then point out that under these circumstances the lesion loses some of its value as a diagnostic test of riboflavin deficiency in population groups. For clinical purposes, however, this finding is not only the most helpful and reliable but the simplest and quickest means of detecting mild riboflavin deficiency. To distinguish it from those instances of vascularization which seem to be caused by other agencies, it is as a rule necessary only

9. Berliner, M. L.: Regarding Early Detection of Avitaminosis A by Gross or Biomicroscopic Examination of Conjunctiva, Am. J. Ophth. **25**: 302 (March) 1942.

10. Patek, A. J., Jr., and Haig, Charles: Effect of Administration of Thyroid Extract and of Alpha-Dinitrophenol on Dark Adaptation, Proc. Soc. Exper. Biol. & Med. **46**: 180 (Jan.) 1941.

11. Boyd, William, quoted by Piersol, G. M.: Arteriosclerosis: Social Significance and Recent Advances in Treatment, Bull. New York Acad. Med. **18**: 36 (Jan.) 1942.

12. Jolliffe, Norman, and Stern, Marvin: Objective Manifestations of Nutritional Deficiency Diseases, Clinics **1**: 282 (Aug.) 1942.

13. Sydenstricker, V. P.; Sebrell, W. H.; Cleckley, H. M., and Kruse, H. D.: The Ocular Manifestations of Ariboflavinosis, J. A. M. A. **114**: 2437 (June 22) 1940. Johnson, L. V., and Eckhardt, R. E.: Rosacea Keratitis and Conditions with Vascularization of Cornea Treated with Riboflavin, Arch. Ophth. **23**: 899 (May) 1940. Sydenstricker, V. P.; Kelly, A. R., and Weaver, J. W.: Ariboflavinosis with Special Reference to the Ocular Manifestations, South. M. J. **34**: 165 (Feb.) 1941.

14. Kruse, H. D.; Palmer, C. E.; Schmidt, W., and Wiehl, Dorothy C.: Medical Evaluation of Nutritional Status: I. Methods Used in a Survey of High School Students, Milbank Mem. Fund Quart. **18**: 257 (July) 1940. Wiehl, Dorothy G., and Kruse, H. D.: Medical Evaluation of Nutritional Status: V. Prevalence of Deficiency Diseases in Their Subclinical Stages, ibid. **19**: 241 (July) 1941.

15. Sebrell, W. H.: Vitamins and Public Health, Fed. Proc. **1**: 319 (Sept.) 1942. Jolliffe, Norman, and Goodhart, Robert: Vitamins in the Practice of Medicine, ibid. **1**: 316 (Sept.) 1942. Youmans, J. B.; Patton, E. W.; Robinson, W. D., and Kern, Ruth, M. S.: An Analysis of Corneal Vascularity as Found in a Survey of Nutrition, 57th annual meeting of Assn. of Am. Physicians, May 5, 1942. Mack, Pauline Berry, and Smith, Janice Minerva: Methods of Conducting Mass Studies in Human Nutrition, Pennsylvania State College Bull., to be published.

16. Youmans, J. B., and Patton, E. W.: The Laboratory Diagnosis of Nutritional Deficiencies, Clinics **1**: 303 (Aug.) 1942.

to consider with it the history, the findings of the physical examination and the results of a therapeutic trial.

The central bilateral ophthalmoplegia of Wernicke's syndrome is due to severe acute thiamine deficiency,[17] but ophthalmoplegias occur from many other causes. Central ophthalmoplegias are common in central nervous system syphilis, multiple sclerosis, basilar meningitis, diphtheritic neuritis and encephalitis.[18] A characteristic bilateral symmetrical polyneuropathy occurs in chronic thiamine deficiency, but a clinically similar polyneuropathy may be due to infectious polyneuritis of the Guillain-Barré type[19] to various intoxicants, to heavy metal poisonings[18] or even to deficiencies of vitamins other than thiamine.[20]

The mucous membrane lesions in and about the mouth[21] present complex diagnostic problems. Some cases showing a magenta glossitis respond to riboflavin,[22] some to pyridoxine[23] and others only to crude liver extract administered parenterally. Cheilosis may appear the same whether due to ariboflavinosis, to edentulous mouth,[24] to allergy or to lipstick. Scarlet fungiform papillae at the tip of the tongue are the earliest visible signs of mild acute nicotinic acid deficiency,[25] but pipe smoking, particularly in persons unaccustomed to a pipe, may produce a similar picture. Vincent's gingivitis and stomatitis may occur in deficiencies of both ascorbic acid and nicotinic acid.[12] This infection becomes active only in the presence of necrotic tissue. Ascorbic acid and nicotinic acid deficiencies are only two of many causes of tissue necrosis in the mouth.

CONDITIONING FACTORS

Following the definition of a conditioned deficiency disease given at the beginning of this paper, the various illnesses and conditions that may produce such deficiencies are listed in tables 3 to 8. It must be emphasized that these tables are not complete but are intended merely to list the more common illnesses, therapeutic measures and physiologic alterations which condition the production of a deficiency syndrome.

Interference with Ingestion.—Strictly speaking, deficiency disease produced by interference with ingestion should not be considered conditioned. Since failure to ingest adequate amounts of food is alone responsible, it would be reasonable to consider these cases as primary deficiencies. Practically, however, in view of the frequency with which disease may interfere with adequate food intake and because of the significance of this classification for preventive therapy, its inclusion as a conditioning factor is warranted. The more common of these conditions are listed in table 3. Gastrointestinal and neuropsychiatric disorders, food allergy and nausea of pregnancy are noted for their interference with food intake, and the literature is replete with references to deficiency diseases developing under these conditions.[2]

In hospitals a meal placed at the patient's bedside is often considered, on the record at least, as eaten, while actually the patient may have consumed little or none of it. Although this may occur under many conditions, it is particularly likely to occur in elderly patients whose hospitalization is more custodial than therapeutic, who may be confused and whose dentures may be in the property room. Within one week 5 such patients with gross deficiency disease have been admitted to my service from "custodial" institutions. Jolliffe, Fein and Rosenblum[26] have recently reported an illustrative case of classic scurvy, pellagra and riboflavin deficiency in a person transferred from a custodial institution where she had been a patient for the previous five years.

Alcohol, though it also produces deficiency disease by other means,[27] may prevent an adequate food intake.

TABLE 3.—*Factors Interfering with Ingestion*

1.	Gastrointestinal disorders Acute gastroenteritis, gallbladder disease, peptic ulcers, diarrheal diseases and obstructive lesions of gastrointestinal tract
2.	Neuropsychiatric disorders Neurasthenia, neurosis, psychoneurosis, psychoses, migraine and neurologic disorders interfering with self feeding
3.	Anorexia Alcohol, operations, anesthesia, infectious diseases, congestive heart failure, thiamine deficiency, visceral pain
4.	Food allergy
5.	Loss of teeth
6.	Pregnancy
7.	Therapy Diets restricting ingestion of essential foods

It does this by replacing other food and by causing nausea and vomiting through its irritant action on the gastric mucosa. This may result in a thiamine deficiency causing anorexia, which in turn results in deficient intake of other nutrients. In this respect thiamine deficiency is frequently the underlying cause of other deficiencies. In some subjects the anorexia caused by lack of thiamine is a protective mechanism guarding the subject against a high caloric intake. However, civilized man on developing anorexia limits his food intake as a rule not to smaller amounts of a balanced diet but to crackers, toast, tea, coffee, sugar and alcohol. With such a diet almost any of the deficiency diseases may develop.

Therapeutic measures often produce deficiency diseases by needlessly restricting the ingestion of certain essential nutritional factors. For example, diets prescribed for patients having allergy, peptic ulcers, biliary disease, nephritis, hypertension, colitis, diabetes or obesity are often deficient in one or more of the essential nutrients. Such diets may occasionally produce more serious disease than the original condition for which the diet was prescribed. Especially harmful are "slimming" diets published in newspapers. Fortunately their low caloric content gives some measure of pro-

17. Jolliffe, Norman; Wortis, Herman, and Fein, H. D.: The Wernicke Syndrome, Arch. Neurol. & Psychiat. **46:** 569 (Oct.) 1941. Wortis, Herman, and Jolliffe, Norman: The Present Status of Vitamins in Nervous Health and Disease, New York State J. Med. **41:** 1461 (July 15) 1941. Alexander, Leo: Beriberi and Wernicke's Hemorrhagic Polioencephalitis, III Cong. Neurol. Internat., Comptes rend. des séances, Copenhagen, Aug. 21, 1939, p. 913.

18. Wechsler, I. S.: A Textbook of Clinical Neurology, Philadelphia and London, W. B. Saunders Company, 1939.

19. De Sanctis, A. G., and Greene, Martin: Acute Infectious Polyneuritis: A Diagnostic Problem During a Poliomyelitis Epidemic, J. A. M. A. **118:** 1445 (April 25) 1942.

20. Wintrobe, M. M.; Miller, M. H., and Falles, R. H., Jr.: What is the Antineuritic Vitamin? Read at the 57th annual meeting of the Association of American Physicians, May 5, 1942.

21. Jeghers, Harold: Nutrition: The Appearance of the Tongue as an Index of Nutritional Deficiencies, New England J. Med. **227:** 221 (Aug. 6) 1942. Martin, Hayes, and Koop, C. E.: The Precancerous Mouth Lesions of Avitaminosis B; Their Etiology, Response to Therapy and Relationship to Intraoral Cancer, Am. J. Surg. **57:** 195 (Aug.) 1942.

22. Sydenstricker, V. P.: Clinical Manifestations of Nicotinic Acid and Riboflavin Deficiency (Pellagra), Ann. Int. Med. **14:** 1499 (March) 1941.

23. Ruffin, J. M., and Smith, D. T.: Pellagra Therapy, Tr. Am. Clin. Otol. A. (1939) **55:** 192, 1940.

24. Ellenberg, Max, and Pollack, Herbert: Pseudoariboflavinosis, J. A. M. A. **119:** 790 (July 4) 1942.

25. Kruse, H. D.: The Lingual Manifestations of Aniacinosis, with Especial Consideration of the Detection of Early Changes by Biomicroscopy, Milbank Mem. Fund Quart. **20:** 262 (July) 1942. Jeghers.[21] Martin and Koop.[21]

26. Jolliffe, Norman; Fein, H. D., and Rosenblum, L. A.: Riboflavin Deficiency in Man, New England J. Med. **221:** 921 (Dec. 14) 1939.

27. Jolliffe, Norman: The Influence of Alcohol on the Adequacy of the B Vitamins in the American Diet, Quart. J. Stud. on Alcohol **1:** 74 (June) 1940.

tection for short periods of time, but, if persisted in, serious damage due to malnutrition may occur. The physician should discourage such unbalanced diets, but if despite advice they are persisted in, a multivitamin preparation, preferably containing the full daily allowances recommended by the Food and Nutrition Board of the National Research Council,[28] should be prescribed. Even well planned reducing diets prescribed by the physician are likely to be short in the B vitamins. For this reason their supplementation with a satisfactory source of these vitamins is desirable. Dried brewers' yeast and extracts of brewers' yeast may be used for this purpose.

Increased Bodily Requirements.—Strictly speaking, malnutrition caused by failure to meet increased bodily requirements need not be considered as conditioned, since it is inadequate ingestion of food that is alone responsible. Practically, however, when the metabolic requirement is increased beyond the usual or average range it is warranted to consider this as a conditioning factor. Fever increases the basal metabolism by 7.2 per cent for each degree F.,[29] while strenuous physical exertion may increase it as much as fifteen times the basal level.[29] The requirement of many nutritive essentials parallels total metabolism whether the change in total metabolism is brought about by physical exertion, disease, environment or drugs. These conditions are listed in table 4.

TABLE 4.—*Factors Increasing Nutritive Requirement*

1.	Abnormal activity, as associated with Prolonged strenuous physical exertion, delirium and certain psychoses
2.	Abnormal environmental factors Excessively high temperatures, as in the tropics, in deserts and in certain industries Excessive light glare as from snow or klieg lights
3.	Fever
4.	Hyperthyroidism
5.	Pregnancy and lactation
6.	Therapy such as thyroid, alpha-dinitrophenol, parenteral dextrose solutions, fever therapy, high carbohydrate diets

The occurrence of deficiency diseases conditioned by fever, hyperthyroidism, pregnancy and lactation are well known. Less well recognized are the effects of abnormal physical activity and unusual environmental factors. Johnson and his collaborators[30] have recently demonstrated an increased requirement of the B vitamins conditioned by moderately strenuous physical activity common to farmers, soldiers and other workers. In a group of men subjected to physical labor equivalent to an output of 4,000 to 5,000 calories, definite deterioration in physical fitness occurred well within one week of starting labor with a diet deficient in the vitamin B complex. Such deterioration could be prevented or cured by the entire B complex containing only 0.6 mg. of thiamine daily but not by 2.0 mg. of thiamine hydrochloride alone. The applicability of these findings to workers in industry, to men in the armed forces and to patients having delirium or a psychosis with pronounced increase in psychomotor activity is obvious.

Sunlight has been recognized as a precipitating agent in pellagra since Gheradini[31] in 1792 produced pellagrous skin lesions on various parts of the body by exposure to the sun. In fact this disease is known among the peasants in Italy as mal del sole. Since the recognition of pellagra in this country, many clinicians[32] have called attention to the possible relationship between exposure to sunlight and the development of the skin lesions. Others[32] have confirmed Gheradini's experiments and in addition have shown that the same exposure in normal subjects leads only to the development of a healthy tan. Furthermore, other trauma, such as radiant energy, dirt, filth and chemical trauma, is believed also to condition nicotinic acid deficient persons to the development of skin lesions.[33] Sunlight not only conditions nicotinic acid deficient persons to skin lesions but is thought by some[34] to play a role in conditioning riboflavin deficient persons to corneal vascularity. Johnson and Eckhardt[13] have demonstrated the effect of sunlight in hastening the onset of corneal vascularization in riboflavin deficient rats, and Sydenstricker, Kelly and Weaver[13] suggest the possibility that prolonged exposure to bright light may cause destruction of riboflavin in the cornea with the production of ocular signs in the absence of lesions elsewhere. Mechanical irritation has been shown to determine the localization of epithelial metaplasia in vitamin A deficiency,[6] while ill fitting dentures and edentulousness which causes caving in of the angles of the mouth may condition the lips to cheilosis.[24]

By increasing total metabolism, various therapies may produce a conditioned deficiency disease. Drugs such as dinitrophenol, thyroxin and thyroid[10] and fever therapy[35] act by increasing metabolism, while parenteral administration of dextrose, insulin shock therapy and high carbohydrate diets act by increasing the requirement for coenzymes without an increase in total metabolism.[36] Many investigators believe that long continued parenteral administration of dextrose is dangerous to patients, particularly those in a borderline state of nutrition. The oxidation and decarboxylation of pyruvic acid, one of the intermediate products of carbohydrate metabolism, requires an enzyme-coenzyme system consisting of a specific protein enzyme (carboxylase), a cocarboxylase (thiamine-pyrophosphate) and magnesium. Other essential components in the mechanism of carbohydrate oxidation include flavoprotein, the dietary precursor of which is riboflavin, coenzymes I and II, the dietary precursor of which is niacin amide, adenosine triphosphate and the iron containing cytochrome system.[36] Bollman[37] has demonstrated that rats partially depleted of their stores of B vitamins and subsequently maintained with dextrose have a longer survival time if thiamine also is administered. No appreciable further effect was noted when the other B vitamins were supplied. Apparently the period of depletion had affected the body stores of thiamine more than it had the other factors of the B complex. Sydenstricker,[22] Jolliffe and Goodhart,[38] and

28. Recommended Allowances for Various Dietary Essentials, Committee on Food and Nutrition, National Research Council, J. Am. Dietet. A. **17:** 565 (June-July) 1941.

29. Duncan, G. G.: Diseases of Metabolism, Philadelphia, W. B. Saunders Company, 1942.

30. Johnson, R. E.; Darling, R. C.; Forbes, W. H.; Brouha, L.; Egaña, E., and Graybiel, A.: The Effects of a Diet Deficient in Part of the Vitamin B Complex on Men Doing Manual Labor, J. Nutrition **24:** 585 (Dec.) 1942.

31. Gheradini, quoted by Harris, Seale; Clinical Pellagra, St. Louis, C. V. Mosby Company, 1941.

32. Reviewed by Harris.[31]

33. Smith, D. T., and Ruffin, J. M.: Effect of Sunlight on the Clinical Manifestations of Pellagra, Arch. Int. Med. **59:** 631 (April) 1937.

34. Kruse, H. D.: Personal communication to the author. Tisdall, F. F.: Personal communication to the author.

35. Daum, Kate; Boyd, Kathryn, and Paul, W. D.: Influence of Fever Therapy on Blood Levels and Urinary Excretion of Ascorbic Acid, Proc. Soc. Exper. Biol. & Med. **40:** 129 (Jan.) 1939.

36. Goodhart, Robert, and Bueding, Ernest: Carbohydrate Metabolism in Practice of Medicine, M. Clin. North America **27:** 315 (March) 1943.

37. Bollman, J. L.: Dextrose Administration and Vitamins B, Proc. Soc. Exper. Biol. & Med. **50:** 18 (May) 1942.

38. Jolliffe, Norman, and Goodhart, Robert: Beriberi in Alcohol Addicts, J. A. M. A. **111:** 380 (July 30) 1938.

Spies [39] have reported the precipitation of deficiency diseases in man by dextrose infusions. Sydenstricker [22] believes that "waterlogging" after the parenteral administration of dextrose and saline solution is more often a manifestation of deficiency than otherwise. The preventive practice of simultaneously administering thiamine, riboflavin and niacin amide along with each dextrose infusion is based on sound theoretical and practical considerations.

Excessive consumption of carbohydrate acts in the same way as parenteral administration of dextrose and there is much evidence in the literature that this is a common method of inducing deficiency diseases.[40] Stepp and Schroeder [41] and Germain, Morvan and Babin [42] have reported instances of beriberi occurring in persons who would have had an adequate thiamine intake except for their unusually high carbohydrate diet. Jolliffe and his co-workers [43] have demonstrated the same phenomenon in alcoholic patients.

Interference with Absorption.—As our knowledge of deficiency diseases increases it becomes more and more evident that disturbances of absorption from the intestinal tract play an important role in the production of deficiency disease. As pointed out by Beams, Free and Glenn,[44] absorption may be impaired because of anatomic, chemical or physiologic changes. These changes are mediated by reduced absorbing surfaces, altered secretions and hypermotility, and further modified by various alkalis, adsorbents and lubricants introduced by the mouth. The more common of these conditioning factors are listed in table 5.

In the diarrheal diseases hypermotility plays the most important role, since the rapid passage of food through the intestinal tract leaves little time for digestion, solution and absorption of the essential factors. In the more chronic diarrheal states, as in sprue or chronic ulcerative colitis, reduction of absorbing surfaces may be equally important. The clinical importance of diarrhea in producing deficiency disease is evidenced by the many recent reports of pellagra, beriberi, scurvy, riboflavin deficiency, vitamin A deficiency, protein deficiency edema and hypocalcemia induced by this conditioning factor.[45]

Achlorhydria may impair the absorption of ascorbic acid [46] and of thiamine.[47] Because of its prevalence particularly in elderly people, achlorhydria always should be suspected in unexplained malnutrition, and malnutrition should be looked for in every subject having achlorhydria.

The role of bile salts in the absorption of the fat soluble vitamins, particularly K, is so well known [48] that it needs only to be mentioned.

The role of vitamin deficiencies themselves in acting as a conditioning factor by impairing absorption is just beginning to be recognized. The intestinal absorption of galactose and probably other sugars is impaired in experimental B complex deficiencies in the rat [49] and in the dog.[50] Groen [51] has shown reduced absorption of dextrose in deficiency states, and Beams, Free and Glenn [44] have also shown impaired absorption of galactose from the intestinal tract in patients suffering from pellagra, sprue and rosacea keratitis. After therapy, absorption returned to normal in the pellagrins and in some of the patients with rosacea keratitis, but in none of the patients with sprue. Lepore and Golden [52] have reported x-ray evidence of a characteristic small intestine lesion in some cases of deficiency diseases which could be cured by B complex therapy. They believe that the impaired absorption was caused by disturbances in motility. Recent reports [53] indicate that carcinoma of the intestinal tract causes defective absorption of vitamin A which can be corrected by B complex therapy.

TABLE 5.—*Factors Interfering with Absorption*

1.	Gastrointestinal diseases associated with hypermotility or reduction of absorbing surfaces
2.	Achlorhydria
3.	Biliary disease, especially obstructive jaundice
4.	Vitamin deficiency
5.	Therapy Liquid petrolatum, colloidal adsorbents, severe catharsis, gastric or intestinal resections and short circuiting operations

Therapy may play an important role in interfering with absorption. Gastrointestinal surgery, particularly resection and short circuiting operations,[54] has long been known to produce macrocytic anemia similar to addisonian pernicious anemia, and there are many case reports to indict it as a factor in the production of

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other deficiency syndromes.[55] Ingestion of liquid petrolatum daily or almost daily is a common practice among many people who are well except for constipation of varying degrees. That such an agent interferes with the absorption of fat soluble vitamins has been indicated by a number of observers.[56]

Interference with Utilization.—This factor is extremely complex and difficult for direct experimental verification. Evidence for interference with utilization is largely circumstantial. In the presence of an adequate intake it is necessary to rule out malabsorption, increased destruction in the bowel, excessive excretion and abnormal requirement before concluding that utilization is defective. It is known for instance that the body must convert carotene to vitamin A, phosphorylate thiamine to cocarboxylase and convert nicotinic acid as its amide to coenzymes I and II, and that riboflavin is essential to more enzyme systems than any other of the known vitamins. Some of these changes may occur in tissue cells in general, but the evidence at this time indicates that the liver is the main organ in which these processes take place. Be that as it may, it is in hepatic disturbances that malutilization is most frequently encountered. In the presence of liver dysfunction these disturbances may be due not only to failure of conversion but to inability of the liver to store [22] a nutrient. The body is then dependent on the day to day intake. This intake naturally varies, with the result that an excess today cannot be stored for a deficit almost certain to occur on some future day.

TABLE 6.—*Factors Interfering with Utilization*

1. Hepatic dysfunction, as in Liver disease, diabetes mellitus, alcoholism
2. Hypothyroidism
3. Malignancy
4. Therapy Sulfonamide drugs, radiation therapy, phenytoin

The more common illnesses associated with impaired utilization are listed in table 6. A tissue deficiency in vitamin A attributable to impaired conversion of carotene to vitamin A has been reported in liver cirrhosis,[57] diabetes mellitus,[58] obstructive jaundice [59] and hypothyroidism.[60] The low plasma levels of vitamin A observed at times in patients having gastrointestinal cancer have been explained as a failure to utilize due to hepatic dysfunction.[53] The high frequency of nutritional diseases in chronic alcohol addicts [61] is well known. Hepatic dysfunction undoubtedly plays a role in these cases. The prevalence of abnormal dark adaptation in hypothyroidism has been thought to imply that the thyroid hormone plays a part in the conversion of the carotene to vitamin A.[60]

Therapy also may interfere with the utilization of vitamins. Although deficiency disease produced by sulfonamide compounds has been attributed mainly to sterilization of the intestinal tract and inhibition of intestinal synthesis of certain factors.[62] West [63] has shown that diarrhea and weight loss in dogs induced by nicotinic acid deficiency and correctable by giving nicotinic acid was not corrected if sulfapyridine was given with the nicotinic acid. On the other hand, raw liver would cure these dogs even in the presence of sulfapyridine, suggesting that sulfapyridine inhibits the action of nicotinic acid but not of the preformed coenzymes present in raw liver. To test out the clinical importance of this finding I have maintained 5 pellagrins in relapse with a basal diet poor in nicotinic acid and administered sulfapyridine in sufficient quantities to obtain a blood level of 8 to 12 mg. One Gm. of sulfapyridine was thereafter administered every four hours, and 400 to 1,000 mg. of nicotinic acid was administered by mouth daily. All the signs and symptoms of pellagra responded as promptly as could be expected if sulfapyridine had not been administered. With the doses of nicotinic acid given (probably excessive) I failed in these few cases to observe any inhibiting effect of sulfapyridine.

Rhoads [64] has produced cancer in susceptible rats by administering a carcinogen. This action was completely prevented by feeding yeast and partially prevented by riboflavin and casein. With in vitro experiments it then was shown that butter yellow blocked the function of coenzyme I. A constituent of this enzyme is nicotinic acid amide. Rhoads concluded "that the administration of at least one carcinogenic chemical injured normal cells by interfering in some way with an enzyme system which is essential for their normal chemical and so their normal life. The results suggested, furthermore, that this principle of the poisoning by a specific chemical of at least one, and possibly more than one, normal enzyme system caused the normal cell to become a cancer cell. . . ." Furthermore, these studies "suggest the necessity of a complete and precise examination of a large number of patients having malignant neoplasms in order to ascertain whether or not they show any evidence of an interference with chemical

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systems of which vitamins form essential compounds." Drake and his co-workers [65] have shown in guinea pigs that phenytoin produces a rapid and progressive fall in the blood ascorbic acid level and recently he [66] has shown that phenytoin lowers the blood ascorbic acid level in human beings. Similarly radiation sickness has been attributed to failure of coenzyme formation from thiamine or nicotinic acid or both.[67]

Increased Excretion.—The role of increased excretion of vitamins in the production of malnutrition has received little attention, although the production of hypoproteinemia by albuminuria, and salt depletion either by excessive sweating or by polyuria, are well known phenomena. The possible factors causing increased excretion are listed in table 7. I know of no case report in the literature in which a vitamin deficiency was thought to be produced solely by this conditioning factor. Cowgill [68] has shown, however, that vitamin B_1 deficiency symptoms appear earlier in dogs maintained with a forced water intake than in dogs that were permitted to drink water ad libitum. He attributed this to increased excretion of vitamin B_1. The possibility of "washing out" the water soluble vitamins must therefore be considered in uncontrolled diabetes mellitus and diabetes insipidus. The loss of vitamins by lactation may be a precipitating factor for deficiency diseases. I have seen 3 patients with severe gestational polyneuropathy who had had only minor symptoms during pregnancy but who rapidly developed severe polyneuropathy during the second week post partum. It was felt that the drain of lactation was the final straw in the pathogenesis of this severe thiamine deficiency.

Methods for determining vitamins in the sweat are technically difficult and not yet satisfactory, so that the practical significance of vitamin depletion by excessive perspiration has yet to be shown convincingly.

By increasing excretion, therapy may contribute to the production of deficiency disease. The forcing of fluids, especially over long periods of time as in certain urinary tract infections, and the loss of fluids by diuresis as in anasarca may be the last straw required to produce a deficiency. Salicylates have been reported [69] to increase urinary excretion of ascorbic acid, but Youmans and his co-workers [70] could not confirm this observation.

Increased Destruction.—Increased destruction of vitamins may occur in the gastrointestinal tract prior to absorption or in the tissues following absorption. The conditioning factors thought to cause increased destruction of vitamins in human beings are listed in table 8. This list does not include either induced thiamine deficiency in animals caused by enzymatic destruction of thiamine by raw carp or of biotin deficiency in man induced by egg white injury, as neither has been shown to occur spontaneously in man, although neither is beyond possibility.

Green [71] and Coombes [72] and their associates have shown thiamine deficiency to be the cause of Chastek paralysis in silver foxes. This deficiency was caused by raw carp, which, when mixed with the food, causes rapid destruction of thiamine. Cooking the carp effectively destroys its ability to inactivate thiamine. It is not known whether any other variety of fish has this ability. I have recently examined four ship-wrecked sailors whose diet for forty-eight days consisted chiefly of raw fish and raw turtle. None of these men showed clinical evidence of thiamine deficiency, and their blood thiamine levels were within normal range.

Induced biotin deficiency in man has been produced experimentally by Sydenstricker and others.[73] He accomplished it by severe dietary restriction plus the feeding of large amounts of raw egg white. The avidalbumin in egg white presumably "fixes" the biotin in the intestinal tract.

The susceptibility of ascorbic acid and thiamine to destruction in alkaline environment has led to some investigation of the role played by achlorhydria and alkaline therapy. Alt, Chinn and Farmer [46] have shown a 65 per cent destruction of ascorbic acid in three hours at a p_H of 7.95, representing achlorhydric gastric juice, and obtained results on patients with achlorhydria suggesting decreased assimilation of ascorbic acid. Kendall and Chinn [74] have obtained from the gastric contents and feces of achlorhydric patients bacteria which destroy ascorbic acid and suggest "that the ascorbic acid fermenting strains may gain the ascendency in the alimentary canal of certain persons, leading in them to a detectable ascorbic acid deficit." Wright and Ludden [46] have also observed signs of vitamin C deficiency in persons with achlorhydria in spite of a

TABLE 7.—*Factors Increasing Excretion*

1.	Polyuria, as in Diabetes mellitus, diabetes insipidus
2.	Lactation
3.	Excessive perspiration
4.	Therapy Long continued excessive fluid intake, as in urinary tract infections

TABLE 8.—*Factors Increasing Destruction*

1.	Achlorhydria
2.	Lead poisoning ?; trinitrotoluene poisoning ?
3.	Therapy Alkalis, sulfonamides, arsenicals

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liberal ascorbic acid intake. They were also able to demonstrate lack of absorption in these subjects after an oral test dose.

Melnick, Robinson and Field [47] have shown that thiamine is stable in gastric juice over a p_H range of 1.5 to 8.0 during sixteen hours of incubation. In the presence of added antiacids the thiamine is completely destroyed, and in the presence of bile or pancreatic juices 50 to 90 per cent was destroyed. The same investigators noted subnormal urinary excretion of a test dose of thiamine in subjects who were given alkalis. Tests in this laboratory by Goodhart [75] also indicate that achlorhydria may interfere with the absorption of thiamine.

Recent investigations indicate that some of the vitamins, particularly ascorbic acid, may play a prominent role in the detoxications. Martin, Fisher and Thompson [76] have reported that ascorbic acid, cystine, aminoacetic acid and calcium gluconate definitely reduced the acute toxic manifestations of sulfanilamide, sulfathiazole and sulfapyridine in rats, while thiamine and nicotinic acid were ineffective. Holmes and his associates [77] have concluded that toxic lead compounds react with ascorbic acid to form a poorly ionized nontoxic salt of lead. The data of Farmer, Abt and Aron [78] indicate that the lowering of plasma ascorbic acid in neoarsphenamine therapy may be the consequence of an attempt on the part of the body to detoxify the drug. The recent findings of Drake [79] on phenytoin, previously discussed in the section on malutilization, also may be explained as a diversion of ascorbic acid to detoxify this drug.

CONCLUDING COMMENT

The term malnutrition signifies not a dietary inadequacy but a tissue deficiency of an essential nutrient. This tissue deficiency may be caused by the failure to ingest an adequate diet. This tissue deficiency may also be caused by factors which interfere with ingestion, absorption or utilization of essential nutrients or by factors that increase the requirement for vitamins, their destruction or excretion. These are known as conditioning factors and when a deficiency disease is produced through their mediation it is known as a conditioned deficiency disease or conditioned malnutrition. The more common illnesses, physiologic factors and therapeutic measures that may produce a conditioned deficiency disease have been listed and briefly discussed. These findings warrant the conclusion that many diseases and some of the therapeutic measures used to combat them interfere with nutrition and are potent factors in the production of deficiency diseases. It is also an inescapable conclusion that the treatment of malnutrition is in each person an individual medical problem requiring exact diagnosis and therapeutic measures which cannot with safety be left in the hands of nonmedical persons. The physician who does so is derelict in his duty to his patient.

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Council on Pharmacy and Chemistry

REPORT OF THE COUNCIL

THE VALUE OF THE XANTHINE COMPOUNDS HAS BEEN DISPUTED ON MANY OCCASIONS. IN 1930 AND IN 1937 (J. A. M. A. **94:** 1306 [APRIL 26] 1930 AND **108:** 2203 [JUNE 26] 1937) THE COUNCIL REVIEWED THE CLAIMS FOR XANTHINE COMPOUNDS IN ORDER TO AID THE MEDICAL PROFESSION IN EVALUATING THE CLINICAL POSSIBILITIES OF THESE AGENTS. TO BRING THIS INFORMATION UP TO DATE, THE COUNCIL HAS AGAIN INITIATED A STUDY OF THE THERAPEUTIC CLAIMS BY ASKING DR. NORMAN H. BOYER TO PREPARE THE FOLLOWING REVIEW OF RECENT WORK ON THIS SUBJECT.

IN AUTHORIZING PUBLICATION OF THIS REPORT THE COUNCIL WISHES TO EXPRESS ITS APPRECIATION TO DR. BOYER FOR HIS REVIEW.

AUSTIN E. SMITH, M.D., Secretary.

AMINOPHYLLINE AND RELATED XANTHINE DERIVATIVES

PRESENT STATUS OF THERAPEUTIC CLAIMS

NORMAN H. BOYER, M.D.

BOSTON

The methyl derivatives of xanthine for which therapeutic claims have been made include caffeine, theobromine and theophylline. The slight solubility of the latter two limits their usefulness, but soluble double salts of either theobromine or theophylline can be formed with a number of compounds. The most widely used combinations are theobromine calcium salicylate or sodium acetate and theophylline ethylenediamine (aminophylline). Caffeine, although the first of the xanthines to be studied and used, has in recent years succumbed to the greater interest shown in theobromine and theophylline. The stimulating effects of caffeine on the central nervous system are somewhat greater than shown by theobromine and theophylline, and its effects on the circulation are definitely less. Theophylline may also produce stimulation of the central nervous system. In addition, the latter drug has the disadvantage of causing gastric and occasionally renal irritation.

DIURETIC ACTION

The value of the xanthines as diuretics dates back to the observations of Babcock,[1] Askanazy,[2] Breuer [3] and Dessauer.[4] These observations have now been amply confirmed; the efficacy of the xanthines as diuretic in congestive heart failure is established. They are usually ineffective when edema is due to extracardiac causes and are inferior in diuretic activity to the mercurial compounds. The convenience of oral therapy often is a distinct advantage of the xanthines.

Diminished dyspnea following the use of xanthines, especially in arteriosclerotic subjects, has been attributed to improvement in collateral coronary circulation,[5] but this is only speculation, and in view of the established diuretic property of these drugs it seems likely that the latter mechanism is the more important one.

Although commonly used as an emergency measure during an attack of paroxysmal dyspnea or acute pulmonary edema due to heart failure, there is no crucial evidence indicating that the xanthines exert any immediate beneficial action under such circumstances. They may, however, be useful in preventing future attacks.

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MYOCARDIAL STIMULATION

Starr and his collaborators [6] found that theophylline when given to patients intravenously increased the cardiac output and left ventricular work without increasing the size of the heart. This was interpreted to indicate myocardial stimulation. The effect of caffeine was in the same direction but of less magnitude and, in the statistical sense, was considered to be insignificant. Boyer and Green [7] found by a totally different method that the xanthines often produced stimulation of the heart and that in this respect the action was similar to epinephrine though less pronounced.

DISEASE OF THE CORONARY ARTERIES

The place of the xanthines in the therapeutics of coronary occlusion and angina pectoris is a subject about which a great deal of controversy and confusion exists. The effects of the xanthines on the coronary arteries, on coronary blood flow and on myocardial infarction has been extensively studied in the experimental animal. In early studies these drugs were observed to produce dilatation of excised coronary arteries. This is obviously a crude, unphysiologic method and does not permit interpretation in terms of clinical medicine or response of the intact animal. Furthermore, the demonstration of dilatation of the large arteries, which lend themselves to such studies, is no criterion of increased flow through smaller arterioles and capillaries. Later methods involving the measurement of outflow from the coronary sinus or coronary inflow by means of the thermostromuhr indicated an increase in coronary flow but have the disadvantage of measuring mean flow only and, furthermore, both methods have been shown to be subject to serious error.[8] Boyer and Green,[7] using a method which allows determination of the flow existing at any moment of the heart cycle, found that the xanthines decreased flow during systole, indicating that the compression of the coronary bed during contraction of the heart was increased. This myocardial stimulation could be shown to precede the increase in total coronary flow, and the suggestion was made that the increase in metabolites liberated in the heart may have produced some or all of the coronary dilatation. Unless it can be shown that the increase in coronary flow is greater than the increase in cardiac metabolism, these drugs cannot be considered effective in increasing the relative blood supply to the heart. The nature of the experiments did not allow the authors to arrive at conclusions on this point. It should be noted that in all reported experimental studies the increase in coronary flow produced by the xanthines has been very transient.

An attempt has been made to discover the effect of the xanthines on myocardial infarction resulting from ligation of a coronary artery in the experimental animal. Fowler, Hurvitz and Smith [9] reported that the extent of cyanosis appearing in an area of the heart acutely deprived of its blood supply was lessened by the administration of aminophylline. Personal experience indicates that such an estimation is extremely difficult. Furthermore, if it does occur it can be attributed to the emptying of venous channels by the increased vigor of myocardial contraction previously referred to, as well as, or better than, to opening of collateral vessels. These authors also estimated that the size of the infarction in dogs killed at intervals of days or weeks following coronary artery ligation and given theophylline with ethylenediamine was smaller than in untreated dogs. Gold, Travell and Modell [10] came to exactly the opposite conclusions by carefully measuring the size of the infarct. Actually the infarcted area in the treated animals averaged 18.3 per cent larger than in similar animals untreated with aminophylline. The authors found it difficult to understand how aminophylline could make matters worse and thought that the difference may have been accidental. There is no denying the possibility of an accidental difference of this magnitude, but it is also possible that the increase in metabolic demands induced by the drug may have had a hand in increasing the size of the infarct. Furthermore, Gold, Travell and Modell found that ventricular tachycardia appeared in 8.7 per cent of the animals untreated with aminophylline, whereas it occurred in 47.4 per cent of the animals receiving the drug. Unfortunately these investigators used cats, while Fowler, Hurvitz and Smith used dogs as the experimental animal. It is, however, extremely unlikely that the divergent results can be accounted for entirely on the basis of species difference. LeRoy, Fenn and Gilbert [11] concerned themselves with the immediate mortality (twenty-four hours) of dogs subjected to ligation of a coronary artery and the effect of drugs on the mortality rate. Under the conditions of their experiments they found an immediate mortality of 70 per cent in untreated dogs. The rate for dogs receiving theobromine with sodium acetate was reduced to 23 per cent and for dogs receiving theophylline was 56 per cent. Considerable doubt may be justifiably raised as to the significance of the reduction (14 per cent) produced by theophylline. The beneficial effects of theobromine sodium acetate, however, appear to be much more definite. Since the immediate mortality is mainly concerned with the onset of cardiac arrhythmias (i. e. ventricular fibrillation) these results are somewhat at variance with those reported by Gold, Travell and Modell. Wiggers and Green [12] were unable to show any immediate favorable effect of the xanthines on blood flow or muscular contraction in an area deprived of its blood supply by coronary artery ligation.

Clinical evaluation of the xanthine drugs in the treatment of coronary artery disease is more important and at the same time much more difficult than determining their effect on experimental animals. The majority of reports in the literature indicate that these drugs are valuable in the treatment of angina pectoris or acute

6. Starr, Isaac; Gamble, C. F.; Margolies, A.; Donal, J. S.; Joseph, N., and Eagle, E.: A Clinical Study of the Action of Ten Commonly Used Drugs on Cardiac Output, Work and Size, on Respiration, on Metabolic Rate and on the Electrocardiogram, J. Clin. Investigation **16:** 799 (Sept.) 1937.

7. Boyer, N. H., and Green, H. D.: The Effects of Nitrites and Xanthines on Coronary Inflow and Blood Pressure in Anesthetized Dogs, Am. Heart J. **21:** 199, 1941.

8. Katz, L. N.; Jochim. K., and Bohning, A.: The Effect of the Extravascular Support of the Ventricles on the Flow in the Coronary Vessels, Am. J. Physiol. **122:** 236 (April) 1938. Katz, L. N.; Jochim, K., and Weinstein, W.: The Distribution of the Coronary Blood Flow, ibid. **122:** 252, 1938. Johnson, J. R., and Wiggers, C. J.: The Alleged Validity of Coronary Sinus Outflow as a Criterion of Coronary Reactions, ibid. **118:** 38, 1937. Shipley, R. E.; Gregg, D. E., and Wearn, J. T.: Operative Mechanism of Some Errors in the Application of the Thermostromuhr Method to the Measurement of Blood Flow, ibid. **136:** 263, 1942. Gregg, D. E.; Pritchard, W. H.; Echstein, R. W.; Shipley, R. E.; Rotta, A.; Dingle, J.; Steege, T. W., and Wearn, J. T.: Observations on the Accuracy of the Thermostromuhr, ibid. **136:** 250, 1942.

9. Fowler, W. M.; Hurvitz, H. M., and Smith, F. M.: Effect of Theophylline Ethylenediamine on Experimentally Induced Cardiac Infarction in the Dog, Arch. Int. Med. **56:** 1242 (Dec.) 1935.

10. Gold, Harry; Travell, J., and Modell, Walter: The Effect of Theophylline with Ethylenediamine (Aminophylline) on the Course of Cardiac Infarction Following Experimental Coronary Occlusion, Am. Heart J. **14:** 284 (Sept.) 1937.

11. LeRoy, G. V.; Fenn, G. K., and Gilbert, N. C.: The Influence of Xanthine Drugs and Atropine on the Mortality Rate After Experimental Occlusion of a Coronary Artery, Am. Heart J. **23:** 637, 1942.

12. Wiggers, C. J., and Green, H. D.: The Ineffectiveness of Drugs on Collateral Flow After Experimental Coronary Occlusion in Dogs, Am. Heart J. **11:** 527, 1936.

coronary thrombosis.[13] However, there is no lack of adverse reports. Gold, Kwit and Otto [14] and Evans and Hoyle [15] concluded that the xanthines exert no specific beneficial action which would justify their use in the treatment of angina pectoris. Those who favor the use of the xanthines have attributed failures to advanced disease of the coronary arteries which is beyond help of any kind, while those who do not believe in the efficacy of the drugs have attributed success in individual cases to placebo-like action. The mere existence of honest differences in opinion suggests that these drugs may be without specific action in the treatment of cardiac pain. Clinical evaluation of the use of any procedure in the treatment of angina pectoris is rendered difficult by the natural course of the disease, with spontaneous remissions and exacerbations, by the subjective nature of the disease and by the many factors which may influence the occurrence of pain. In order to obviate or control some of these factors, objective measurement of the effect of the xanthines has been attempted. Brown and Riseman [16] used the response to a standard exercise test as a criterion for the effect of the xanthines on the amount of work which could be accomplished before pain was induced. Unfortunately this report gives no actual figures for the amount of work performed before and after the administration of the drugs but simply the percentage of patients "improved." They reported improved exercise tolerance in 31 per cent of patients treated with theobromine and 54 per cent treated with theophylline. When these xanthines were combined with sodium acetate the number of patients showing improvement increased to about 80 per cent.

Number of Trips Without Medication and After Aminophylline

No Treatment	Aminophylline 3 Grains (0.2 Gm.) Four Times a Day
20—32	29
26—40	23
16—23	16
26—31	22
30—44	54
33—34	57
34—42	35
8—11	10
31—40	44

In another report Riseman and Brown [17] claimed that aminophylline improved the exercise tolerance by as much as 100 per cent. Such improvement must have been exceptional, for a table giving the actual number of trips over a two step platform gave the figures reproduced herewith.

This is certainly not impressive evidence for improvement. Only 2 of the 9 patients according to the suggestive evidence presented in their table were able to tolerate more exercise after the administration of aminophylline than before. In evaluation of the treatment of a disease as variable as is angina pectoris much more striking results should be demanded before therapeutic claims are made. Levy, Bruenn and Williams [18] tested the effect of aminophylline on the occurrence of pain and on electrocardiographic changes induced by breathing a low oxygen mixture in patients with coronary artery disease. They found that aminophylline intravenously increased the duration of anoxemia tolerated before pain appeared by an average of approximately four and one-half minutes (63 per cent) and decreased the average arithmetical ST segment deviation by approximately 2.2 mm. (50 per cent). Aminophylline by mouth was less effective and, on the average, increased the duration of tolerated anoxemia by a little over two minutes (26 per cent) and decreased the average ST segment changes by 1.4 mm. The evidence presented by these figures is suggestive but certainly not conclusive. The number of patients tested was small (10) and the average differences produced by aminophylline administered orally is not so great as to preclude some doubt as to their significance. It should also be noted that of ten tests with intravenous aminophylline 1 patient experienced pain after a shorter period of breathing the low oxygen mixture than when in the untreated state.

CHEYNE-STOKES RESPIRATION

Hot black coffee is a time honored respiratory stimulant, and caffeine has long enjoyed a reputation of effectiveness in the treatment of periodic breathing. Recently the other xanthine compounds have been utilized and studied with regard to their effectiveness. Marias and McMichael [19] reported that intravenous aminophylline was almost always effective in restoring rhythmic breathing but that frequently the effect was transient, especially when the irregular respiration was associated with severe heart failure or with head injuries or intracranial hemorrhage. In other cases the effect of a single injection lasted hours or even permanently abolished the respiratory arrhythmia. The authors attributed the favorable action of aminophylline to direct stimulation of the respiratory center, since they found no change in pulse rate, blood pressure or cardiac output to indicate central circulatory stimulation. As was previously indicated, the experience of other investigators is not in accord with the latter findings. Marias and McMichael inferred that the action of the drug did not depend on dilatation of the cerebral blood vessels with consequent improvement in blood supply to the respiratory center because of the observation that aminophylline increases pulmonary ventilation in normal subjects. It was assumed by the authors that a drug which enhanced the removal of metabolic products from the respiratory center would tend to depress respiration in normal persons. An increase in both rate and depth of respiration in normal subjects by aminophylline has been confirmed and the suggestion made that the drug be routinely used to prevent postoperative atelectasis.[20]

Nathanson and Fitzgibbon [21] also found aminophylline to be effective in the treatment of Cheyne-Stokes

13. LeRoy, G. V.: The Effectiveness of the Xanthine Drugs in the Treatment of Angina Pectoris, J. A. M. A. **116:** 921 (March 8) 1941. Massel, H. M.: Clinical Observations on the Value of Various Xanthine Derivatives in Angina Pectoris, J. Lab. & Clin. Med. **24:** 380 (Jan.) 1939. Gilbert, N. C., and Kerr, J. A.: Clinical Results in Treatment of Angina Pectoris with the Purine Base Derivatives, J.A.M.A. **92:** 201 (Jan. 19) 1929. Smith, Rather and Paul.[5] Brown and Riseman.[16]

14. Gold, Harry; Kwit, N. T., and Otto, Harold: The Xanthines (Theobromine and Aminophylline) in the Treatment of Cardiac Pain, J. A. M. A. **108:** 2173 (June 26) 1937.

15. Evans, W., and Hoyle, C.: The Comparative Value of Drugs Used in the Continuous Treatment of Angina Pectoris, Quart. J. Med. **26:** 311, 1933.

16. Brown, M. G., and Riseman, J. E. F.: The Comparative Value of Purine Derivatives in the Treatment of Angina Pectoris, J. A. M. A. **109:** 256 (July 24) 1937.

17. Riseman, J. E. F., and Brown, M. G.: Medicinal Treatment of Angina Pectoris, Arch. Int. Med. **60:** 100 (July) 1937.

18. Levy, R. L.; Bruenn, H. G., and Williams, N. E.: The Modifying Action of Certain Drugs (Aminophylline, Nitrites, Digitalis) on the Effects of Induced Anoxemia in Patients with Coronary Insufficiency, Am. Heart J. **19:** 639, 1940.

19. Marias, O. A. S., and McMichael, J.: Theophylline Ethylenediamine in Cheyne-Stokes Respiration, Lancet **2:** 437, 1937.

20. Speiling, L.; Weisman, S., and Papermaster, R.: The Effect of Intravenous Theophylline with Ethylenediamine (Aminophylline) on the Rate and Depth of Respiration, Surgery **11:** 600, 1942.

21. Nathanson, M. H., and Fitzgibbon, J. P.: Pharmacology of Cheyne-Stokes Respiration, Am. Heart J. **17:** 691, 1939.

respiration. When given intravenously its action was immediate and the effect often lasted for hours. In some instances oral medication with aminophylline was also thought to be helpful.

BRONCHIAL ASTHMA

In 1921 theobromine and theophylline were shown to have a bronchodilator action on excised pig bronchi.[22] This observation has recently been confirmed by Young and Gilbert,[23] who also used isolated bronchi. The latter authors found that aminophylline exerted a protective action against bronchial constriction produced by histamine, that ethylenediamine alone is ineffective, and that the action of aminophylline was a direct one on the bronchial muscle. More recently Luduena,[24] using the whole animal, also confirmed the bronchodilator effect of theophylline derivations. Not only did the xanthines produce dilatation of "normal" bronchi, but they overcame, in variable degree, bronchoconstriction produced by histamine, barium, pilocarpine and anaphylaxis. The xanthines were inferior to epinephrine by a very large margin (1,000 to 2,000 times). In pithed dogs a similar though less pronounced effect of the xanthines was observed, indicating that action on the central nervous system is not an essential factor in its efficacy. The author attributed the decreased effectiveness in the pithed animal to poorer general condition of animals so treated. When animals were given moderate doses of the xanthines over a period of weeks, no microscopic changes could be demonstrated in the tissues. However, when larger doses were administered over a period of weeks, slight microscopic changes were observed in the meninges and kidneys.

Meanwhile these drugs had been found useful in the clinical treatment of bronchial asthma,[25] finding their greatest field of usefulness for patients who had become unresponsive to epinephrine. The clinical usefulness of aminophylline in the treatment of bronchial asthma has been confirmed by a large number of clinicians whose opinions have not found their way into the literature.

HYPERTENSION AND PERIPHERAL VASCULAR DISEASE

No careful clinical study of the effects of xanthines on hypertension has appeared, but it is the general consensus that these drugs are without value in reducing high blood pressure.

In 1934 Scupham[26] reported that clinically the xanthines appeared to do good in some cases of some kinds of peripheral vascular diseases. It was absolutely ineffective in Raynaud's disease and in acrocyanosis. It seemed to help some cases of thromboangiitis obliterans or arteriosclerotic vascular disease. Unfortunately most of the cases reported by this author were hospitalized and other forms of recognized treatment for vascular disease were administered.

McGovern, McDevitt and Wright,[27] using skin temperature changes as a criterion and administering large doses of theobromine with sodium salicylate (2.6 Gm.) by mouth, concluded that this drug was too feeble and unreliable a vasodilator to be of value in the treatment of peripheral vascular disease. Stewart and Jack[28] measured peripheral blood flow by changes in the thermal conductance of the skin. By this method aminophylline produced an increase in peripheral blood flow of 40 to 195 cc. per square meter of body surface per minute in eighteen to twenty-five tests. The effect was always transient and this fact, together with doubts related to the method used, renders the report of questionable value in demonstrating that aminophylline is a valuable therapeutic agent in the treatment of peripheral vascular disease.

SUMMARY

1. The xanthine derivatives are useful diuretics in congestive heart failure. The diuretic action of theophylline is somewhat more intense but less lasting than theobromine compounds. The latter give rise to less gastric irritation than do theophylline compounds, although enteric coating minimizes this difference. There is no satisfactory evidence to show that these drugs exert an immediate action which justifies their use in acute pulmonary congestion or edema.

2. The xanthines stimulate the myocardium to increased vigor of contraction: this is accompanied by increased cardiac output and increased work of the heart.

3. Increased coronary blood flow produced by theophylline in the experimental animal follows, rather than precedes, the myocardial stimulation. Until it can be shown that the increase in coronary flow is disproportionately large in comparison to the increase in cardiac metabolism, the experimental basis for the clinical use of theophylline in increasing the blood supply to the heart must rest on insecure ground. Evidence that the xanthines exert a favorable influence on experimental myocardial infarction is inconclusive but seems slightly in favor of the absence of any such favorable action.

4. Clinical evaluation of the usefulness of the xanthines in the treatment of coronary artery disease is far from satisfactory. It seems wise to place the burden of proof on those who claim therapeutic efficacy, and the evidence presented so far does not seem altogether unequivocal. Reports based on the evaluation of the subjective accounts of patients is open to serious errors, and attempts to determine the objective effect of these drugs, while commendable, are not beyond criticism. The employment of accepted statistical methods in arriving at conclusions although not compensating for poor methods or controls would do much in clarifying the significance of such studies.

5. The xanthines are useful in the treatment of Cheyne-Stokes respiration. At times the effect is transient but in other cases the effect may last several hours.

6. Aminophylline is effective in the treatment of bronchial asthma; it finds its greatest field of usefulness in patients who have become epinephrine fast. In general it is less effective than epinephrine and should not supplant the latter.

7. There is no basis for claims that the xanthines effectively reduce high blood pressure.

8. The available evidence is opposed to claims that these drugs are useful in the treatment of peripheral vascular disease.

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25. Herman, G., and Aynesworth, M. B.: Successful Treatment of Resistant Extreme Dyspnea, "Status Asthmaticus," J. Lab. & Clin. Med. **23:** 135, 1937. Lamson, R. W., and Bacon, L. C.: Theophylline Monoethanolamine: A Critical Study of Its Use in the Treatment of Asthma and Other Allergies, J. A. M. A. **116:** 915 (March 8) 1941.
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27. McGovern, T.; McDevitt, E., and Wright, I. S.: Theobromine Sodium Salicylate as a Vasodilator, J. Clin. Investigation **15:** 11, 1936.
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SATURDAY, MAY 29, 1943

IODINE AND THE THYROID

Since 1895, when Baumann discovered iodine in thyroglobulin, a protein isolated from the thyroid, this element has been closely associated with the physiology of the gland. Most of the 30 to 40 mg. of iodine in the body is localized in the thyroid, whose tissue has extraordinary ability to fix and retain iodine.[1] Thyroxin and diiodotyrosine are the two iodine-containing compounds which have been isolated from the hydrolysis products of thyroid protein. However, they account for only about two thirds of the total iodine in the gland, the nature of the combination of the remainder being unknown.

Recent studies have thrown light on the ability of iodized proteins to simulate thyroxin activity. Krauss and Monroe[2] produced a remission of experimental hyperthyroidism through the use of iodized milk. Therapeutic effects of iodized whole serum protein have been demonstrated in human patients with athyrosis[3] and similar results which have been described in guinea pigs treated with iodized casein.[4] The chemotherapeutic pattern of stimulation by these artificially iodized proteins is probably the same as when desiccated thyroid is used, as shown by successful isolation of thyroxin from the hydrolysis products of iodized casein.

Some indication of the pathway of synthesis of the thyroid hormone has been provided by recent experiments in which radioactive iodine was employed. Mann and his co-workers[6] injected radioactive iodine into dogs, and the relative amounts of inorganic iodine, diiodotyrosine and thyroxin in the thyroid substance were calculated from the relative specific radioactivities of these fractions. From the data these investigators concluded that diiodotyrosine seems to be the precursor of thyroxin. Data which might be taken as support for this conclusion were secured by Morton and Chaikoff[7] from in vitro experiments. Slices of thyroid from dogs, rats and sheep were incubated in a nutrient medium containing radioactive iodine. The medium was then hydrolyzed and both diiototy rosine and thyroxin which contained the labeled iodine were isolated. The relative proportion of the added radioactive iodine appearing in the two compounds which varied in the different species of animals were such as to indicate that there is a close relationship between the dioodotyrosine and the thyroxin.

The observations here reported emphasize the close qualitative chemical and functional relationship between the thyroid protein and artificially iodized proteins. Quantitatively the thyroid protein is much more potent than the iodized protein thus far prepared. Nevertheless here is the possibility of preparing this active therapeutic agent in the laboratory or on a large scale. With respect to the mode of formation of the thyroid hormone, suggestive evidence is at hand through the use of radioactive iodine.

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2. Krauss, W. E., and Monroe, C. F.: J. Biol. Chem. **89:** 581 (Dec.) 1930.
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5. Ludwig, W., and von Mutzenbecher, P.: Ztschr. f. physiol. Chem. **258:** 195 (April 25) 1939. Harington, C. R., and Rivers, R. V. P.: Nature **144:** 205 (July 29) 1939.
6. Mann, Walter; Leblond, C. P., and Warren, S. L.: J. Biol. Chem. **142:** 905 (Feb.) 1942.
7. Morton, M. E., and Chaikoff, I. L.: J. Biol. Chem. **147:** 1 (Jan.) 1943.

ALLERGIC TUBERCULOSIS IMMUNITY

Widely accepted views as to the relationship between allergy and immunity in tuberculosis are challenged by Woodruff and Kelly[1] of the Detroit Tuberculosis Sanatorium. In a recent summary Rich[2] concluded that allergy is not a necessary accompaniment of an effective immunity in any infectious disease. This conclusion was based largely on experiments[3] which indicated that allergic guinea pigs given desensitizing doses of tuberculin are able to withstand subsequent infection with highly virulent strains of tubercle bacilli as well as control guinea pigs left in their original hypersensitive state. This result is of practical clinical interest, since it suggests that tuberculin therapy is without deleterious effects.

Subsequently Willis[4] questioned the experimental basis for this conclusion, since he found that there was but slight difference between allergic and desensitized guinea pigs if given massive test doses of highly virulent tubercle bacilli but that the results were quite different with smaller or less virulent doses. With doses that allow the injected animals to remain alive for at least six months, a 100 per cent mortality of the tuberculin desensitized animals took place long before all nondesensitized controls had died. Moreover, in the desensitized animals the lungs were almost

1. Woodruff, C. E., and Kelly, R. G.: J. Immunol. **45:** 79 (Oct.) 1942.
2. Rich, A. R.: Physiol. Rev. **21:** 70 (Jan.) 1941.
3. Cummings, D. E., and Delahaut, A. B.: Tr. Nat. Tuberc. A., 1934, p. 123.
4. Willis, H. S., and Woodruff, C. E.: Am. J. Path. **14:** 337 (May) 1938.

completely hepatized by tuberculous pneumonia, with little or no involvement of the liver or the spleen. In the allergic controls the pulmonary involvement was minimal, the spleen being the organ showing the maximum predilection to the disease. Lack of acquired allergy was apparently responsible for the free and unrestrained growth of tubercle bacilli in the desensitized lungs.

During the past three years 218 normal guinea pigs have been infected subcutaneously with fatal doses of virulent human tubercle bacilli in the Detroit Laboratory and tested quantitatively for skin sensitivity throughout the course of the disease. In all cases the acquired skin sensitivity increased to a maximum in about four to five weeks. After this the animals could be divided into two groups. In one group the skin sensitivity decreases rapidly after the fifth week, the animals becoming desensitized by about the twelfth week, which spontaneous desensitization was invariably followed by death. On necropsy extensive pulmonary involvement was noted with enormous numbers of tubercle bacilli in the lungs. In the other group the acquired skin sensitivity was not decreased but increased slightly above the five week level. These durallergic animals remained alive well beyond the fourteenth week and on etherization showed but few acid fast bacilli in pulmonary sections or smears.

From such data Woodruff and Kelly conclude that a quantitative relationship between skin sensitivity and pulmonary resistance to tuberculosis exists, nonallergic or spontaneously desensitized pulmonary tissues favoring a profuse local proliferation of the tubercle bacilli. Spontaneous desensitization is demonstrated also in human tuberculous patients.

Current Comment

VENEREAL DISEASE IN THE NAVY

For approximately thirty years, as was mentioned in a previous comment,[1] gonorrhea has consistently remained either in first or in second place among the leading causes of morbidity in the Navy. The over-all admission rate for the entire Navy, according to Lang, was 60.61 per thousand for this disease alone. Especially encouraging, therefore, is the report of Comdr. T. J. Carter [2] on the figures for venereal disease admission to the Navy for the years 1940 through 1942. From these it appears that for the Navy the rate for all venereal disease was 80 per thousand in 1940, was 51 in 1941 and was about 36 in 1942. These figures represent decreases of 36 per cent between 1940 and 1941 and of 29 per cent between 1941 and 1942. The trend is downward by 55 per cent over the three year period. In the suppression of the spread of the infection, the "place of exposure" assumes real importance. Analysis of the 1942 cases reveals that ten leading cities alone are the source of 41 per cent of all cases in the Navy about which data are available. These ten cities likewise account for 57 per cent of the venereal disease cases originating in the United States. During 1942 only 28 per cent of the Navy venereal disease problem came from foreign ports. Thus the bulk of the problem will remain in the United States for some time to come. The measures proposed by the Special Committee on Enforcement of the National Advisory Police Committee on Social Protection may bring about an even further reduction in these figures.

1. Epidemiology of Gonorrhea and the Navy, Current Comment, J. A. M. A. **120:** 926 (Nov. 21) 1942.
2. Carter, T. J.: Statement on Venereal Disease in the U. S. Navy, 1942, read before the Special Committee on Enforcement of the National Advisory Police Committee on Social Protection, Washington, D. C., April 2, 1943.

PREVENTION OF SULFADIAZINE CRYSTALLURIA

A method of preventing "renal irritation" (crystalluria) following sulfadiazine therapy is suggested by detailed studies of the solubilities of sulfadiazine and its conjugation products reported by Gilligan and his colleagues [1] of Cornell University Medical College. Previous clinical data [2] have shown that the incidence of sulfadiazine crystalluria is higher in acid than in neutral or alkaline urines, suggesting the possibility that precipitation of sulfonamide excretion products in the renal tubules is determined by the p_H level. To test this theory large amounts of acetylsulfadiazine were added to phosphate buffer solutions ranging in p_H from 5.2 to 8.0. The mixtures were shaken for eighteen hours in a water bath at 37 C. and then filtered at the same temperature. Analyses of the resulting filtrates by the Bratton technic [3] showed an acetylsulfadiazine solubility of about 10 mg. per hundred cubic centimeters at p_H 5.2, increasing to about 60 mg. at p_H 6.5. With alkaline urines (p_H 7.5) the solubility was over 500 mg. per hundred cubic centimeters, a ten to fifty times greater solubility than in acid buffer solutions. Similar data were obtained with free or uncombined sulfadiazine. Clinical studies suggested by these data revealed a 27 per cent incidence of crystalluria following sulfadiazine therapy in 172 cases of acid urine. In 147 urines previously rendered alkaline by oral administration of sodium bicarbonate, only 2 specimens showed crystals. Both cases cleared on further administration of sodium bicarbonate. The conclusion was drawn that sulfadiazine crystalluria can be prevented in all cases by oral administration of this alkali. The dosage necessary to maintain the urine at an alkaline level is, of course, variable. From 13.7 to 19.5 Gm. daily, given in six divided doses, is suggested by the Cornell clinicians. This amount is well tolerated and does not give clinical evidence of alkalosis. In renal or cardiac insufficiency Gilligan suggests that such amounts may be contraindicated. Whether or not prophylactic urinary alkalization modifies the therapeutic efficiency of sulfadiazine has not yet been determined.

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2. Schwartz, Leon; Flippin, H. F.; Reinhold, J. G., and Domm, A. H.: The Effect of Alkali on Crystalluria from Sulfathiazole and Sulfadiazine, J. A. M. A. **117:** 514 (Aug. 16) 1941.
3. Bratton, A. C., and Marshall, E. K., Jr.: New Coupling Component for Sulfanilamide Determination, J. Biol. Chem. **128:** 537 (May) 1939.

SYMPOSIUM ON RELATIONS OF MEDICINE AND LAW

The Department of Legal Medicine of the Harvard Medical School has announced its sponsorship of a symposium series on scientific proof and relations of medicine and law. The papers comprising the series, fifty-three in number, deal with clinical forensic medicine, forensic pathology, scientific crime detection, modes and mechanisms of scientific proof, medical criminology, expert testimony, private and public law problems of interest to physicians and other equally important interrelationships between medicine and law. Arrangements have been made for a wide publication of the papers in a number of medical and law journals, some of which are devoting entire issues to the symposium. To enable those interested to know in what journals the individual papers are published, a master index to the series has been prepared in booklet form.[1] This symposium represents an ambitious and intelligent effort to clarify some of the problems in which medicine and the law have common interests and to illustrate the breadth of the field in which such problems arise. It should arouse a keener interest in and a fuller understanding of a subject that deserves more thoughtful consideration by both physicians and lawyers than has been given it in this country.

MOSQUITO VECTORS AND ANIMAL RESERVOIRS OF ENCEPHALITIS VIRUSES

Since the outbreak of encephalitis in St. Louis in 1933, other outbreaks have been recognized as predominantly due to the same virus. Significant observations have resulted from recent field and laboratory studies on this subject in the Yakima Valley, Washington. Both St. Louis and western equine viruses have been isolated repeatedly from one species of mosquito there, Culex tarsalis Coq. Antibodies to both viruses have been found in 50 per cent of apparently healthy domestic fowl in that area and also in a high proportion of fowl in other areas. The question was whether this mosquito would become infected and infective with each of these two viruses as the result of feeding on domestic fowl. Hammon, Reeves and Gray [1] report the results of their attempt to reproduce in the laboratory this hypothetical cycle believed to occur naturally (mosquito-fowl-mosquito). They fed fowl on blood virus suspensions and demonstrated transmission not only by Culex pipiens and Culex coronator as previously reported but also by three other genera of mosquitoes and a tick. Probably in at least one epidemic area (Yakima Valley) both St. Louis and western equine encephalitis viruses were mosquito borne, and the source of mosquito infection was a huge inapparent reservoir among domestic fowl and possibly other vertebrates. Apparently control should be directed primarily at the arthropod vectors, with human vaccination also under special circumstances.

1. This index may for a brief time be procured from the Editor-in-Chief of the symposium, Dr. Hubert Winston Smith, Langdell Hall, Harvard Law School, Cambridge, Mass., for 15 cents plus 1½ cents postage.

1. Hammon, W. McD.; Reeves, W. C., and Gray, M.: Mosquito Vectors and Inapparent Animal Reservoirs of St. Louis and Western Equine Encephalitis Viruses, Am. J. Pub. Health **33**: 201 (March) 1943.

ELECTROCARDIOGRAPHIC CHANGES WITH EXERCISE

In a series of electrocardiographic investigations of normal persons, Barrow and Ouer [1] observed the effects of vigorous participation in various sports and correlated the results with the factors of age, smoking and cardiovascular stability as measured by the Schneider index. The observations were performed on a series of 100 normal men on whom electrocardiographic changes were produced by vigorous participation in such active sports as handball and badminton. Tracings were taken immediately before and immediately after exercise. Significant changes in the auriculoventricular or the intraventricular conduction time were not observed. Inversion of the P wave in lead CF_4 after exercise occurred in about half the group. Changes in the T wave were common, but frank inversion of this wave or distortion of the ST segment was not found. A change in the size of the QRS complex was most common, being found in four fifths of the men in the series. Half of the men studied were under 40 years of age, averaging 31, while the other half were over 40, averaging 49. Significant electrocardiographic differences between the two age groups, however, were not found. Similarly a definite difference in the average rating of the two age groups could not be determined by the Schneider index. Three fifths of the men were smokers; they had a Schneider index slightly lower than the nonsmokers. The effects of exercise on the whole were thus not particularly striking, though the authors state that one should be suspicious of intrinsic myocardial damage when distortion of the ST segment or frank inversion of the T wave in significant leads is produced by exercise. Perhaps it is safe to believe that in the majority of instances the legs or other elements of the musculoskeletal system would tend to give out before the heart, thereby serving as a factor of safety.

PROBLEMS OF CONVALESCENCE

The Subcommittee on Clinical Investigation of the National Research Council has decided to bring the problems of convalescence to the attention of investigators and clinicians throughout the country. What is the real nature of convalescence? Why is it frequently prolonged after the fever subsides? Why must there be a period of gradual recuperation after trauma or major surgery? These are problems suggestions in regard to which, with proposals for investigation, are invited. The military importance of these problems is evident when one considers the number of casualties and the importance of prompt rehabilitation for active duty. The value of a better understanding of convalescence in all forms of medical practice is obvious. Suggestions with regard to investigative projects in the field of convalescence should be sent to the Subcommittee on Clinical Investigation, National Research Council, 2101 Constitution Avenue, Washington, D. C.

1. Barrow, W. H., and Ouer, R. A.: Electrocardiographic Changes with Exercise, Arch. Int. Med. **71**: 547 (April) 1943.

MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on War Participation of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war and such other information and announcements as will be useful to the medical profession.

ARMY

WITH GENERAL CHENNAULT IN BURMA AND CHINA

Two years ago while serving as a flight surgeon in North Carolina, Lieut. Col. Thomas C. Gentry, M. C., U. S. Army, was called to Washington to discuss with Capt. Claire L. Chennault, a retired air corps officer with whom he had previously served, proposed plans for organizing a volunteer group for duty along the Burma Road and in China. Lieutenant Colonel Gentry was authorized by special authority of China's minister, Dr. T. V. Soong, to hire the necessary personnel to care for about three hundred specialists who were to make up the American Volunteer Group and to buy medical supplies sufficient for twelve months' service in the orient. He bought a portable x-ray unit, surgical instruments and supplies, blood plasma, antimalarial drugs, vitamins and thirty hospital beds. The medical staff was to include a general surgeon, an orthopedic surgeon, an internist, an eye, ear, nose and throat specialist, a dental officer, two female nurses, one male nurse, a flight surgeon's assistant, a dental technician, one ambulance driver and two first aid men. In the *Military Surgeon* for May Colonel Gentry states that, although malaria has taken a terrible toll for centuries in northern Burma and southwestern China, not a single death due to illness occurred in the American Volunteer Group "during the year we spent in Burma and China." While the Burma Road was under construction, thousands of workmen died of malaria and two commissions were sent out by the U. S. Public Health Service to supervise antimalarial work. The excellent health of the American Volunteer Group is attributed to the physical condition maintained by every member, who even in the extreme heat of Burma engaged in outdoor athletics to the amazement of the natives; also to the fact that all members of the group fully cooperated with the medical members and came to them early when illness developed. Many a pilot in this group owes his life to his physical condition, which enabled him to endure repeated air raids and to walk back many miles to his base after forced landings. Eight pilots were lost in accidents incident to routine training flights, only five were actually shot down in combat, seven were killed by fire from the ground while on bombing missions and three others were captured during raids over the enemy lines. The Americans with one hundred planes destroyed five hundred Japanese planes. Flying fatigue became a menace when replacements which had been promised did not arrive and it became necessary for the fliers to stand alert for long periods with no days off. In order that some pilots especially in need of rest might have an excuse for leave from combat duty, Lieutenant Colonel Gentry says that elective operations were performed on a few. This group arrived in Rangoon on Aug. 15, 1941 and the U. S. Army Air Forces took over the American Volunteer Group on July 4, 1942. New personnel and equipment then came from home, although about forty veterans of the American Volunteer Group remained with their gallant leader, now Major General Chennault.

TWO HUNDRED FLIGHT NURSES

The Army Air Force Air Evacuation Group at Bowman Field, Louisville, Ky., held graduating exercises recently for a class of two hundred flight nurses who, on the following morning, staged a demonstration, including the rapid conversion of a transport plane into a hospital plane, the removal of wounded from an advanced airdrome and the nursing treatment of wounded during flight. Brig. Gen. David N. W. Grant, the air surgeon, addressed the class and presented the diplomas.

THE STATION HOSPITAL AT FORT LEONARD WOOD

The Station Hospital at Fort Leonard Wood, Missouri, celebrated its second anniversary on May 3. Fort Leonard Wood, one of the largest army posts in the country, located deep in the Ozark Mountain section of Missouri, has a vast hospital with a capacity of about 2,250 beds occupying some 200 acres of rolling countryside.

The commanding officer, Col. Leeson O. Tarleton, Medical Corps, a graduate of Harvard University in the class of 1910, is serving not only as commanding officer of the hospital but also as station surgeon.

The present staff includes 69 officers, 155 nurses, 677 enlisted men and 208 civilians. As of May 1 the professional staff of the hospital was as follows:

ADMINISTRATIVE SERVICE

Col. Leeson O. Tarleton, commanding officer and station surgeon.
Major Arthur E. Putz, executive officer.
Major Robert A. Murray, assistant executive officer, registrar and receiving and disposition officer.

SURGICAL SERVICE

Col. Millard F. Arbuckle, chief of surgical service.
Major Ronald F. Elkins, chief of proctology section.
Major Richard E. Speirs, ward surgeon.
Major George F. Swanson, ward surgeon.
Capt. Raymond E. Cooper, chief of anesthesia section.
Capt. Thomas E. Ferrell Jr., chief of clean surgery section.
Capt. Donald A. Kendall, assistant chief of surgery service.
Lieut. Vernon G. Watters Jr., chief plastic surgery section.

(ORTHOPEDIC)

Major Wesley H. Burnham, chief of orthopedic section.
Capt. James F. Kennedy, thoracic surgeon.
Capt. Hanns C. Schwyzer, chief of chest surgery section.
Lieut. Melville Rosenbusch, chief of physical therapy section.

(EYE, EAR, NOSE AND THROAT)

Lieut. Col. Leander T. Simons, chief of eye, ear, nose and throat section.
Major William F. Boiler, chief of ear, nose and throat subsection.
Capt. Marshall Y. Soldineer, bronchoscopist.
Lieut. Stanley S. Chunn, ward surgeon.
Lieut. Robert B. Stump, ophthalmologist.

MEDICAL SERVICE

Lieut. Col. Neville E. Stewart, chief of medical service.
Major Charles R. McAdam, assistant chief of medical service.
Major Armand W. Hanss, chief of officers' and nurses' section.
Major Howard J. Lee, chief of general medicine section.
Major Franklin O. Meister, ward surgeon.
Capt. Robert A. Coen, ward surgeon.
Capt. Jacob W. Fleming Jr., chief of gastroenterology section.
Capt. Delmar R. Gillespie, cardiologist.
Capt. Emil C. Mrozek, chief of dermatologic section.
Capt. Ingall H. Neas, assistant chief of neuropsychiatric section.
Capt. Philip W. Smith, chief of urology section.
Capt. Howard A. Stellner, ward surgeon.
Lieut. Usher L. Frankel, ward surgeon.
Lieut. Otto E. Ramik, ward surgeon.
Lieut. John M. Rhodes, ward surgeon.
Lieut. Walker M. Turner, ward surgeon.
Lieut. Mervyn H. Williams, ward surgeon.

RADIOLOGY SERVICE

Lieut. Col. Weaver A. Rush, chief of radiology service.
Major Loira C. Pumphrey, assistant chief of radiology.

OUTPATIENT SERVICE

Capt. Carl L. Mangiameli, chief of outpatient service.

LABORATORY

Capt. Miles E. Foster Jr., chief of laboratory service.
Capt. Julius H. de Mackiewicz, assistant chief of laboratory.
Capt. Myron S. Silverman, bacteriologist.

SPECTACLES FOR ENLISTED MEN

The Adjutant General's Office, Washington, D. C., issued the following memorandum on May 11:

1. Pamphlet No. 8-5, War Department, 1943, consolidates all previous instructions and regulations concerning issuance of spectacles, changes the basis of issue and provides substantially that enlisted men will be issued two pairs of spectacles, if authorized, as soon as possible after date of induction. This issuance will be made at the home station without regard to movement overseas.

2. Until such time as the effect of the instruction contained in Pamphlet No. 8-5 is achieved, and in the exceptional cases which will arise thereafter, training center commanders are permitted to ship replacements to depots with only one pair of spectacles when time does not otherwise permit. The prescription for obtaining the additional pair of spectacles will accompany the records of the enlisted man to the depot, and action will be initiated at that station to have the prescription filled. Personnel will not be detained at depots for lack of these spectacles; the additional pair will be forwarded to them at their proper oversea address.

BRIG. GEN. GRANT CONTINUES AS AIR SURGEON

In a realinement of the functions of headquarters components of the Army Air Forces, designed to decentralize control, announced recently by the War Department, the offices of headquarters are reduced from twenty-five to thirteen and there will be six major components of the air staff instead of nineteen as formerly. The headquarters staff of Gen. Henry H. Arnold, Commanding General, Army Air Forces, includes among others a chief of air staff, Major Gen. George E. Stratemeyer, three deputy chiefs and six assistant chiefs of air staff. A new Office of Special Projects has been created and a new commandant, Army Air Forces, Flight Control Commandant, formed. Major Gen. Follet Bradley, who has been on special duty at headquarters, Army Air Forces, becomes Air Inspector, and Brig. Gen. David N. W. Grant, continues as Air Surgeon.

FORMER COLONEL WEARS LIEUTENANT BARS

The maximum use of available manpower and the placement of skilled but aged persons is illustrated in the case of a former colonel who wears a lieutenant's bars in order to qualify for an assignment. Dr. Philip S. Potter, pediatrician, had in twenty-four years' work advanced to the rank of colonel in the Medical Reserve Corps, which he entered on discharge as a captain when he returned from France in 1918. While the present war was about to leave him on the sidelines the 68 year old physician was confident that he could serve. While he has not been called to active duty as a colonel, his experience is being used by the Army at the California Quartermaster Depot, where he now serves as a first lieutenant and thus releases a younger medical officer for duty with troops.

POSTHUMOUS AWARD OF DISTINGUISHED SERVICE CROSS

Lieut. Victor H. Karpass of the U. S. Army Medical Department was awarded the Distinguished Service Cross posthumously, according to the Chicago *Daily News* of April 7, for heroism during the invasion of Algeria last November 2. Lieutenant Karpass, it is said, refused to abandon ship and in the midst of an operation on a wounded sailor he was struck by an enemy shell and killed. Lieutenant Karpass was 33 years of age and a graduate of the University of Illinois School of Medicine, Chicago.

THE FIRST DENTIST PARACHUTE JUMPER

Lieut. Herbert O. Eppleman of the U. S. Army Dental Corps, who recently graduated from the Parachute School at Fort Benning, Ga., was the first officer of the dental service to qualify as a parachute jumper. Lieutenant Eppleman was assigned to duty with the 503d Parachute Infantry Regiment.

AVIATION MEDICAL EXAMINERS

Another class of aviation medical examiners graduated on March 11. Graduation exercises were held at the School of Aviation Medicine in Texas and at the three army air forces classification centers, where the practical portion of the course was conducted. Following is a list of the students graduated:

ALABAMA

Andrew D. Henderson, Captain, Mobile.
Benjamin F. Jackson Jr., Captain, Montgomery.
William H. Spruell, 1st Lieut., Russellville.

ARIZONA

Delbert W. Hess, 1st Lieut., Tucson.
William P. Holbrook, Lieut.-Col., Tucson.
Meyer M. Mandel, 1st Lieut., Tucson.

ARKANSAS

Lucas M. Bryd Jr., 1st Lieut., Little Rock.
Milton C. John Jr., 1st Lieut., Stuttgart.
Ely D. Rowland, Captain, Hot Springs National Park.
Carl R. Williams, 1st Lieut., Morrilton.

CALIFORNIA

William L. Argo, 1st Lieut., Oakland.
Anthony G. Badami, 1st Lieut., San Jose.
Richard O. Bagley, 1st Lieut., San Francisco.
Louis H. Bassett, 1st Lieut., San Diego.
Daniel W. Boudett, 1st Lieut., San Francisco.
Robert B. Case, 1st Lieut., Oakland.
Ralph Chapman, 1st Lieut., Los Angeles.
Harry S. Chong, 1st Lieut., Berkeley.
David Clithero, 1st Lieut., Los Angeles.
Charles B. Craycroft, 1st Lieut., San Jose.
Paul H. Cronenwett, 1st Lieut., Alameda.
Roger W. Hackley, 1st Lieut., Oakland.
Howard Hammond Jr., 1st Lieut., San Rafael.
Brace F. Hartwell, 1st Lieut., Orange.
Robert M. Ireland, 1st Lieut., Los Angeles.
Julius Lewis, 1st Lieut., Berkeley.
Frank C. Melone, 1st Lieut., Ontario.
John W. Moore, 1st Lieut., Quincy.
Leslie S. Orleans, 1st Lieut., Los Angeles.
Aaron E. Oswald, 1st Lieut., Bakersfield.
Max L. Salvator, 1st Lieut., Sacramento.
Ralph V. Sloan, 1st Lieut., Glendale.
Richard A. Warrick, 1st Lieut., Los Angeles.
Don E. Woodard, 1st Lieut., Oakland.
Ney J. Zahry, 1st Lieut., Bakersfield.

COLORADO

Herbert V. Temple, 1st Lieut., Haybro.

CONNECTICUT

Joseph B. Hanley, 1st Lieut., Terryville.
Mayo R. Purple, Captain, New Haven.

DELAWARE

Walter E. Gunby Jr., 1st Lieut., Seaford.

DISTRICT OF COLUMBIA

Philip A. Cox, 1st Lieut., Washington.
Milton Morton Greenberg, Captain, Washington.
Norman B. Kanof, 1st Lieut., Washington.
Alfred J. Krug, 1st Lieut., Washington.
Oliver K. Niess, Lieut.-Col., Washington.
Richard K. O'Loughlin, 1st Lieut., Washington.

FLORIDA

Karl B. Hanson, Captain, Jacksonville.
Lloyd H. Jennings, 1st Lieut., Starke.
Joseph L. G. Lester Jr., 1st Lieut., Miami.
Frederick P. Poppe, 1st Lieut., Coral Gables.
Raymond R. Sessions, 1st Lieut., Kissimmee.
Willett E. Wentzel, 1st Lieut., Bradenton.

GEORGIA

Joseph L. Berg, 1st Lieut., Augusta.
William D. Jarratt, Captain, Macon.

IDAHO

John R. Mangum, 1st Lieut., Nampa.

ILLINOIS

Walter Pope Alvis, 1st Lieut., Evanston.
Melbourne W. Boynton, Major, Chicago.
John G. Ersfeld, 1st Lieut., Chicago.
John P. Kieffer, Captain, Chicago.
James O. Lawrence, 1st Lieut., Chicago (Evanston).
Isadore Lerner, 1st Lieut., Chicago.
Barney Malbin, 1st Lieut., Chicago.
Wiley R. Marvel, 1st Lieut., Weldon.
Wesley B. Oliver, 1st Lieut., Belvidere.
Samuel B. Prevo, Major, Marshall.
Donald J. Reichert, 1st Lieut., Evanston.
Julius B. Richmond, 1st Lieut., Chicago.
Jack H. Sloan, Captain, Chicago (Highland Park).
William B. Smith, 1st Lieut., Grand Ridge.
Grant Suttie, 1st Lieut., DeKalb.
Gilbert Alphon Towle, 1st Lieut., Chicago Heights.
Lawrence E. Woodard, Captain, Evanston.
Gordon W. Wormley, 1st Lieut., Rockford.

INDIANA

George W. Dyer, 1st Lieut., Terre Haute.
Gordon H. Haggard, Major, Indianapolis.
August M. Hasewinkle, 1st Lieut., Fort Wayne.
Francis P. LaFata, 1st Lieut., Gary.
Gilbert G. Lapid, 1st Lieut., East Chicago.
Arthur D. McKinley, 1st Lieut., Speedway.
James S. Murray Jr., 1st Lieut., Indianapolis.
Harold E. Ropp, Captain, New Harmony.
Karl W. Vetter, 1st Lieut., Elkhart.
Ralph C. Wilmore, 1st Lieut., Indianapolis.

IOWA

Paul D. Bruns, 1st Lieut., Des Moines.
Jesse L. Cochran, 1st Lieut., Carrol.
Richard D. Crow, 1st Lieut., Shreveport.
Thomas R. Dolan, 1st Lieut., Greene.
Johann L. Ehrenhaft, 1st Lieut., Iowa City.
Henry H. Gurau, 1st Lieut., Des Moines.
Robert H. Harris, 1st Lieut., Mason City.
Joseph L. Ptacek, 1st Lieut., Webster City.
Lee E. Rosebrook, 1st Lieut., Ames.
James W. Standeven, Captain, Oakland.

KANSAS

Spencer H. Boyd, 1st Lieut., Topeka.
Samuel T. Coughlin, Major, Larned.
James G. Gaume, 1st Lieut., Ellinwood.
Edwin R. Hill Jr., Major, Lyons.

KENTUCKY

Shelby G. Bale, Captain, Elizabethtown.

Robert W. Bushart, Captain, Fulton.
Walter R. Byrne, Captain, Russellville.
Arch M. Carr, 1st Lieut., Middlesboro.
Paul E. Harper, 1st Lieut., Dry Ridge.
William M. Townsend, 1st Lieut., Falmouth.

LOUISIANA

James E. Ball, 1st Lieut., Shreveport.
Orien E. Dalton, 1st Lieut., New Iberia.
John F. Daniel, 1st Lieut., New Orleans.
John S. Herring, Captain, New Orleans.
Charles Sypert Holt Jr., 1st Lieut., Shreveport.
Edward Perry Thomas, Captain, New Orleans.
Lee Williamson, 1st Lieut., New Orleans.

MAINE

Philip B. Thomas, 1st Lieut., Bangor.

MARYLAND

Joseph M. George Jr., 1st Lieut., Sudlersville.
William N. Horsley, 1st Lieut., Baltimore.
Saul J. Robinson, 1st Lieut., Baltimore.

MASSACHUSETTS

Joseph A. Daly, 1st Lieut., Natick.
Harry L. Day, Captain, Worcester.
Samson Fisher, Captain, Revere.
Ray S. Gilmore, 1st Lieut., Lowell.
Bernard Rapoport, 1st Lieut., Boston.
Norman Simon, 1st Lieut., Lawrence.
Roger N. Violette, 1st Lieut., Fall River.
James F. Whitten, 1st Lieut., Amesbury.

MICHIGAN

Donald K. Barstow, 1st Lieut., St. Louis.
Thornton I. Boileau, 1st Lieut., Detroit.
George E. Clark Jr., 1st Lieut., Detroit.
George R. Clinton, 1st Lieut., Mason.
Theodore R. Florentz, 1st Lieut., Detroit.
Edward H. Lass, 1st Lieut., Oxford.
Harold A. Machin, 1st Lieut., Kalamazoo.
Paul H. Muske, 1st Lieut., Detroit (Dearborn).
William G. Robinson, 1st Lieut., Hart.
Gerald Rottschafer, 1st Lieut., Detroit.
Marion A. Sapala, 1st Lieut., Detroit.
John P. Williams, 1st Lieut., Detroit.

MINNESOTA

Joseph E. Frank, Captain, Marshall.
John L. Noble, 1st Lieut., St. Paul.

MISSISSIPPI

Bert R. Burgoyne, 1st Lieut., Laurel.
Richard A. Street Jr., Captain, Vicksburg.

MISSOURI

Edward J. Becker, 1st Lieut., Clayton.
David R. Edwards, 1st Lieut., St. Joseph.
Herbert C. Sweet, 1st Lieut., Koch.
William L. Topp, 1st Lieut., St. Louis.

NEBRASKA

Henry G. Crellin, Captain, Lyons.

NEW HAMPSHIRE

Gardner F. Manning, 1st Lieut., Manchester.
Charles E. Moors Jr., 1st Lieut., Rochester.
Marc E. Richard, Captain, Dover.

NEW JERSEY

Robert E. Bennett, 1st Lieut., Palmyra.
Francis J. Benz, 1st Lieut., Chatham.
Jerome M. Cebula, 1st Lieut., Jersey City.
William Paxson Chalfant Jr., 1st Lieut., Ventnor.
Edward M. Coe, 1st Lieut., Union City.
James R. Eynon, Lieut., Collingswood.
Anthony J. Girardo, 1st Lieut., Berlin.
Eugene L. Miller, 1st Lieut., Newark.
Edwin J. O'Brien, 1st Lieut., Plainfield.
Daniel H. Stephenson, 1st Lieut., Camden.
Baxter H. Timberlake, Major, Atlantic City.

NEW MEXICO

Leland Sparks Evans, Captain, Las Cruces.
William A. Glasier, 1st Lieut., Carlsbad.
Walter S. Smith, 1st Lieut., Pinehaven.

NEW YORK

Jesse Appel, 1st Lieut., New York.
Daniel D. Argentieri, 1st Lieut., Brooklyn.
John F. Argue, 1st Lieut., Wilson.
George J. Baron, 1st Lieut., Rochester.
Karl H. Behm, 1st Lieut., Westbury.
Gerald J. Booken, 1st Lieut., New York.
Natale G. Brunetta, 1st Lieut., New York.
Earl E. Conaway, 1st Lieut., Brooklyn.
Joseph G. Constantino, Captain, Ozone Park.
Arthur C. Davis, 1st Lieut., Glens Falls.
Aaron R. Edwards, 1st Lieut., Ithaca.
Wade B. Ellis, Captain, Buffalo.
Jacob S. Garber, Captain, Jamaica.
Maurice A. Golden, 1st Lieut., Long Island City.
Frederick W. Goodrich, 1st Lieut., Catskill.
Murray J. Hanigsberg, 1st Lieut., Elmhurst.
James G. Harrity, 1st Lieut., Buffalo.
Joseph H. Healy, 1st Lieut., Brooklyn.
Edward J. Keegan, 1st Lieut., Oneonta.
John E. Lally, 1st Lieut., New York.
Anthony J. Leone, 1st Lieut., Ithaca.
Robert W. Lipsett, 1st Lieut., Buffalo.
Brahm A. Mandour, 1st Lieut., Utica.
Albert D. Meacham, 1st Lieut., Binghamton.
Francis J. Murray, 1st Lieut., New York.
Daniel J. O'Connor, Major, New York.
Theodore F. Paprocki, 1st Lieut., Bay Shore.
Robert Park Jr., 1st Lieut., Manhassett.
Brittain F. Payne, Major, New York.
Morris R. Rapoport, 1st Lieut., New York.
Leslie B. Roberts, 1st Lieut., New York.
Beryl D. Rosenberg, 1st Lieut., Richmond Hill.
Emanuel Roth, 1st Lieut., Brooklyn.
Lester D. Rothman, 1st Lieut., New York.
Jack Sang, 1st Lieut., New York.
William Sapsin, 1st Lieut., Canton.
Arthur G. Schwartz, 1st Lieut., Rome.
George F. Seelinger, 1st Lieut., Williston Park.
William G. Self, 1st Lieut., Brooklyn.
Meyer Silvert, 1st Lieut., Bronx.
Carl B. Smith, 1st Lieut., Victor.
Jacob M. Sobel, 1st Lieut., New York.
Lawrence L. Spitzer, 1st Lieut., New York.
Albert M. Tocker, 1st Lieut., Brooklyn.
Marvin Weinberg, 1st Lieut., New York.
Aaron S. Weston, 1st Lieut., Brooklyn.
Irwin W. Winfield, 1st Lieut., New York.
Lawrence B. Winkelstein, 1st Lieut., New York.

NORTH CAROLINA

Lemuel U. Creech, 1st Lieut., High Point.
Harry S. Hickman, 1st Lieut., Hudson.
Frank R. Mann Jr., 1st Lieut., Durham.
Lundie C. Ogburn, Captain, Winston-Salem.
Homer H. Price, 1st Lieut., Draper.

NORTH DAKOTA

Robert G. McCurdy, Captain, Bismarck.

OHIO

James D. Apple, 1st Lieut., Dayton.
Paul Victor Bartos, 1st Lieut., Columbus.
Ord C. Blackledge, 1st Lieut., East Cleveland.
Christopher A. Colombi, 1st Lieut., Lakewood.
William C. Craig, 1st Lieut., Columbus.
John H. Dornheggen, 1st Lieut., Cincinnati.
Joseph C. Forrester, Captain, Columbus.
Samuel K. Gerson, Captain, Lancaster.
Thomas M. Hayes, 1st Lieut., Springfield.
Philip T. Knies, Major, Columbus.
Jones C. Laughlin, 1st Lieut., Cleveland.
George H. Lemon, 1st Lieut., Fayette.
Harvey A. Lewis, 1st Lieut., Cleveland.
George Macatee Jr., 1st Lieut., Cleveland.
Morris B. Martin, 1st Lieut., Springfield.
Theodore R. Mattocks, 1st Lieut., Marietta.
Allen P. Newman, 1st Lieut., Toledo.
Charles J. Prochaska, Major, Lyndhurst.
Frederick R. Scroggin, 1st Lieut., Cincinnati.
Trent W. Smith, 1st Lieut., Norwood.
Henry Spitzer, 1st Lieut., Cleveland.
Byron C. Stuhlman, 1st Lieut., Dayton.

OKLAHOMA

George T. Allen, Captain, Oklahoma City.
Murray M. Cash, 1st Lieut., Tulsa.
John R. Curry, 1st Lieut., Blackwell.

OREGON

Neil F. Black, Captain, Klamath Falls.
Paul Metz, 1st Lieut., Portland.
Douglas Q. Thompson, 1st Lieut., Pendleton.
Herman F. Vehrs, 1st Lieut., Portland.

PENNSYLVANIA

Richard A. Caldwell, 1st Lieut., Pittsburgh.
Benjamin Dickstein, 1st Lieut., Philadelphia.
Arthur J. Fischer, 1st Lieut., Pittsburgh.
Morton Joshua Freedman, 1st Lieut., Philadelphia.
Jacob H. Garber, 1st Lieut., Elizabethtown.
William W. Glass, 1st Lieut., Philadelphia.
Homer A. Graham, 1st Lieut., Pittsburgh.
John R. Groh, 1st Lieut., Philadelphia.
Edgar S. Highberger, 1st Lieut., Greensburg.
Benjamin W. Jenkins, 1st Lieut., Philadelphia.
Bernard M. Kalstone, 1st Lieut., McKeesport.
Anthony J. Kameen, 1st Lieut., Forest City.
Allen R. Kannapel, Captain, Lehighton.
Eugene F. Lester Jr., 1st Lieut., Erie.
Paul D. McGehee Jr., 1st Lieut., Philadelphia.
Thomas J. McKenna, 1st Lieut., Blaunox.
James P. Proudfit, 1st Lieut., Washington.
Edward C. Raffensperger, 1st Lieut., Philadelphia.
Philip A. Schifalacqua, 1st Lieut., Philadelphia.
Willard D. Stewart, 1st Lieut., Pleasantville.
Robert S. Stricker, 1st Lieut., Wilkes-Barre.
Paul J. Whitaker, 1st Lieut., Pittsburgh.
Edward J. Wiater, 1st Lieut., Reading.
Harold N. Yoh, 1st Lieut., Reading.
Dale E. York, 1st Lieut., Philadelphia.

RHODE ISLAND

Richard S. Arlen, Captain, Providence.
Edwin B. Gammell, 1st Lieut., Hope Valley.
William A. McDonnell, 1st Lieut., Providence.

SOUTH CAROLINA

Charles B. Sadler, 1st Lieut., Charleston.
John Westley Speake, 1st Lieut., Spartanburg.

SOUTH DAKOTA

Roland F. Hubner, 1st Lieut., Yankton.

TENNESSEE

John W. Anderson, 1st Lieut., Nashville.
Ralph D. Ashbaugh, 1st Lieut., Nashville.
Glen R. Johnson, Captain, Memphis.

TEXAS

Woodrow M. Avent, 1st Lieut., Cameron.
Cecil M. French, 1st Lieut., Dallas.
Woodson W. Harris, 1st Lieut., Houston.
Ernest E. Lowrey, 1st Lieut., Gatesville.
John Q. Rounsaville, 1st Lieut., Houston.
Oscar O. Selke Jr., 1st Lieut., Houston.
George Y. Siddons, 1st Lieut., Fort Worth.
Howard P. Wheeler, 1st Lieut., Georgetown.
Neul C. Windrow Jr., 1st Lieut., Houston.

UTAH

Abram H. Cannon, 1st Lieut., Salt Lake City.

VIRGINIA

Donald L. Arey, 1st Lieut., Danville.
Nathaniel T. Ballou Jr., 1st Lieut., Fredericksburg.
Robert H. Detwiler, Captain, Arlington.
John N. Dunn, Captain, Blackstone.
Robert B. Mallett, Captain, Orange.

WASHINGTON

Clarence W. Bledsoe, 1st Lieut., Seattle.
Walter C. Cameron, Major, Tacoma.
Donold R. Crow, 1st Lieut., Seattle.
Gordon C. Hackett, 1st Lieut., Longview.
Ralph H. Highmiller, Captain, Olympia.
John D. Way, 1st Lieut., Seattle.
Melvin J. Wirz, 1st Lieut., Seattle.

WEST VIRGINIA

Emory H. Main, 1st Lieut., Philippi.
Charles R. Morris, 1st Lieut., Wheeling.
John F. Stecker, 1st Lieut., Morgantown.

WISCONSIN

Robert E. Callan, 1st Lieut., Wauwatosa.
Willard E. Klockow, 1st Lieut., Muscoda.
William H. Schuler, 1st Lieut., Fenimore.
Paul N. Seebohm, 1st Lieut., Madison.

WYOMING

Franklin D. Yoder, 1st Lieut., Cheyenne.

NAVY

IOWANS DONATE EQUIPMENT TO NEW BATTLESHIP

The Medical and Surgical Relief Committee of America has presented the new 45,000 ton battleship U. S. S. *Iowa* with six emergency field sets, six operating kits and other medical supplies with a total value of more than $3,000. Dr. Walter L. Bierring, health commissioner of Iowa and chairman of the Iowa division of the Medical and Surgical Relief Committee, said that the committee has received further requests from the *Iowa*. All kinds of dental instruments are urgently needed as well as one hundred operating gowns, transfusion apparatus and other medical supplies. Dr. Harry Hurd of Des Moines is launching a campaign to raise funds to meet the dental needs of the *Iowa*. All funds raised will be turned over to the new battleship and where possible equipment purchased by Iowans will carry a plaque inscribed with the name of the donor. Contributions should be sent to the Iowa representatives of the Medical and Surgical Relief Committee, Dr. Walter L. Bierring, Dr. Harry Hurd and Dr. Robert L. Parker of Des Moines, Dr. Rose L. Butterfield of Indianola, Iowa, or directly to the committee headquarters, 420 Lexington Avenue, New York.

MEDICAL KITS FOR PATROL BOATS

The Woman's Auxiliary to the Kent County Medical Society, Grand Rapids, Mich., residents of Cleveland and others contributed funds for the purchase by the Medical and Surgical Relief Committee of America, 420 Lexington Avenue, New York City, of ten emergency medical kits for the coast guard patrol boats of the Ninth Naval District at Cleveland. This is the first of a shipment of fifty kits to patrol boats of the thirteen naval districts of the coast guard and to the submarine chasers of the Navy. These portable medical kits are filled with essential drugs and emergency instruments and are complete enough to cope with casualties until the ship reaches a base hospital. Detailed instructions are included in the kit so that it may be used by the pharmacist's mate or other members of the crew in the absence of a physician. The kit also contains mirrors for signaling, a simple fishing outfit and bait, and vital tools in case the crew has to take to the life rafts.

To equip emergency medical kits, the Medical and Surgical Relief Committee of America has launched a salvage campaign urging women and sportsmen to collect small knives, especially wooden handled knives, scissors, tweezers, mirrors, bandages and safety pins, and discarded fishing lines, reels, hooks and sinkers. The committee requested all physicians who attended the recent annual meeting of the New York State Medical Society in Buffalo to bring with them any spare or discarded instruments and surplus drugs as a contribution to this and other phases of its work. The medical members of the National Advisory Committee of the Medical and Surgical Relief Committee include Rear Admiral Ross T. McIntire, Surgeon General, U. S. Navy, Dr. Stuart L. Craig, Lieut. Comdr. Carnes Weeks, Dr. Conrad Berens, Dr. Joseph Felson, Dr. Morris Fishbein, Dr. Franz Groedel, Dr. Malcolm Goodridge, Dr. Crenshaw D. Briggs and Dr. Marjorie E. Reed.

LIEUT. RITTER A PRISONER OF THE JAPANESE

Mrs. Edward F. Ritter, Mattoon, Ill., has been officially informed, it is reported, that her son, Lieut. Edward F. Ritter Jr. of the U. S. Navy Medical Corps, is a prisoner of the Japanese in the Philippine Islands. Lieutenant Ritter graduacted from Harvard and received his M.D. degree from Northwestern University Medical School in 1938. After serving a year's residency at Passavant Hospital, Chicago, he was transferred to a Naval hospital in New York and was sent to the Philippine Islands about a year and a half before the attack on Pearl Harbor.

NAVY CROSS AWARDED TO DR. PRATT

Lieut. Comdr. Theodore C. Pratt, MC, U.S.N.R., on leave of absence from the surgical staff of the Massachusetts General Hospital and of the Palmer Memorial Hospital, has been awarded the Navy Cross "for extraordinary heroism and distinguished service in line with his profession as chief surgeon of a division field hospital on Guadalcanal." The citation states that Dr. Pratt courageously operated on and supervised treatment of casualties while the hospital was being bombed by enemy planes and shelled by surface craft during last August and September.

CIVILIAN DEFENSE

OFFICE OF CIVILIAN DEFENSE ADVISES GAS CLEANSING STATIONS AT HOSPITALS

Hospitals should make complete plans for the immediate establishment, when needed, of "gas cleansing stations" for the care of injured persons who have been exposed to war gases, the Medical Division of the Office of Civilian Defense advised on May 25 in Operations Letter No. 124 (Supplement No. 4 to Operations Letter No. 42). Large communities should establish at least one gas cleansing station without delay for training purposes.

The OCD recommends that the term "gas cleansing" be used to describe the procedure of removing vesicant liquids from persons and that the term "decontamination" be reserved for areas and objects.

The primary purpose of gas cleansing stations is the protection of hospitals and casualty stations and their staffs and patients from contamination by injured persons who have been exposed to vesicant agents, the operations letter points out. Contaminated persons who are not disabled are expected to cleanse themselves in the nearest private home or in other local facilities.

Existing facilities in casualty receiving hospitals must be converted into gas cleasing stations, it is pointed out, since, under present conditions of scarcity of materials and manpower, construction of new facilities is generally not justified. Hospital facilities that should prove suitable are suggested as follows: hydrotherapy rooms, nurses' or interns' locker and shower rooms, part of the outpatient department, garages or other separate structures. In the event that these are not available, facilities to care for persons who are both injured and contaminated must be arranged in schools, gymnasiums, swimming pools, shower rooms, club houses and community centers.

Cleansing stations should be equipped to take care of one third to one half of the hourly casualty receiving capacity of the hospital to be served, the OCD recommends. The professional staff will consist of mobile medical teams assigned when the station is activated, supplemented by additional attendants from the Emergency Medical Service. In addition to cleansing and emergency treatment, the staff of the gas cleansing station will assist in undressing the injured, moving stretchers caring for clothing and valuables, maintaining supplies and dressing wounds.

It is recommended that cleansing stations be established at or near hospitals and casualty stations which they are to serve. Every hospital that may be required to handle an appreciable number of casualties should have access to such cleansing station facilities.

The local chief of Emergency Medical Service is responsible for the development of these stations, with the advice of the senior gas officer of the community.

MISCELLANEOUS

ARMY-NAVY E AWARDS

Brig. Gen. Fred W. Rankin of the Surgeon General's Office and President of the American Medical Association made the presentation of the flag at ceremonies at which the Army-Navy E Production Award was made to the Seamless Rubber Company, New Haven, Conn., and Capt. Reynolds Hayden, medical officer of the Third Naval District, presented the E insignia to representatives of the employees of the company.

In recognition of the volunteer services of Nassau County physicians in the blood donor work conducted by the Nassau County Red Cross, the Army-Navy E award which the blood donor unit has been given was forwarded on March 30 to the Nassau County Medical Society in Mineola, N. Y. Local physicians are in constant attendance at all blood donor sessions, which are scheduled in villages throughout the county. The time schedules are arranged so that physicians relieve one another when necessary, but one doctor at least is always present to conduct the necessary examinations.

The following additional industrial plants have been granted the Army-Navy E award for outstanding performance on war work: the Cleveland Dental Manufacturing Company, Cleveland; the Norwich Pharmacal Company, Norwich, N. Y.; M & R Dietetic Laboratory, Inc., Columbus, Ohio; Armour and Company and the Armour Laboratories, Union Stockyards, Chicago; The Kelley-Koett Manufacturing Company, Covington, Ky. E. R. Squibb and Sons of Brooklyn and New Brunswick, N. J., who were granted the Army-Navy E award in September 1942, have added a star to their E pennant as an outward symbol of the renewal for another six months of this award.

Hynson, Westcott & Dunning, Inc., Baltimore, manufacturers of drugs, and its employees, were presented with the Army-Navy E Award in ceremonies held at the Hotel Belvedere in that city on April 12.

DETROIT RANKS SECOND IN BLOOD DONATIONS

Although fourth in population among American cities, Detroit stands second in its volume of blood donations. The chairman of the Detroit Blood Donor Service Committee is Frederick S. Stearns, chairman of the board of Frederick Stearns & Company, a Detroit drug manufacturing concern. Mr. Stearns became chairman of the Blood Donor Station in January 1942, and by mid-April the number of donors in the Detroit area had reached 162,153. March, a record month, saw 24,181 volunteers donate 21,298 pints of blood. Mr. Stearns has organized volunteer groups in many manufacturing plants. Three mobile blood donor units cover the metropolitan area within 40 miles of Detroit, and these are booked solidly up to July. A substation at the Ford River Rouge plant processes an average of 200 donors a day. Blood donor honor rolls are prominent on the walls of this plant and there is interdepartmental rivalry for the highest donor total. Chairman Stearns credits the Detroit record to the application of a well known merchandising principle: correct treatment of the "customer" so that he keeps coming back. Of the 21,000 donors in March of this year, more than 9,000 of them had previously donated blood.

MEDICAL AND SURGICAL RELIEF COMMITTEE

The Medical and Surgical Relief Committee of America, 420 Lexington Avenue, New York City, shipped fourteen medical field sets last month to nine Caribbean ports to aid in the medical care of the survivors of torpedoed ships, and twenty-two more emergency medical field sets are ready for shipment by the committee to other Caribbean ports. In its three years of work, which is conducted by a nationwide group of physicians, the Medical and Surgical Relief Committee of America has distributed more than a half million dollars worth of medical and surgical supplies to the people and fighting forces of the United Nations. The medical director of the committee is Dr. Joseph P. Hoguet.

RUSSIAN WAR RELIEF, INC.

Shipments from Russian War Relief, Inc., with headquarters at 11 East Thirty-Fifth Street, New York, to the Soviet Union left American ports in the first quarter of 1943 at the rate of $1,000,000 a month, and the total of medical supplies, clothing, foods, seeds and knit goods up to March 31 of this year had a value of more than $3,000,000, and in addition the organization had relief supplies on hand awaiting shipment or in transit, purchase commitments and records of previous shipments which amounted to nearly $5,000,000 as of March 31. While, since the inception of this corporation in 1941, Russian War Relief has shipped and entered into purchase commitments for goods valued at nearly $8,000,000, Edward C. Carter, president of the relief agency, told the board of directors in New York, April 26, that the bank reserve and incoming cash, contributions and war chest allocations of the relief agency are being used to purchase supplies requested by Soviet authorities as quickly as they can be ordered or found available.

INNOVATORS OF SCIENCE

GRIGORY SHAKHOV

[NOTE.—*By cable from Russia comes the following account of medical progress in Russia.*—ED.]

Col. Alexei Maximenkov of the Red Army Medical Service spent the bitter winter of 1941-1942 in Leningrad finishing scientific work to which his teacher had devoted a good half of his long life.

Neither incessant enemy air raids nor artillery bombardments, neither hunger nor cold prevented him from working with a group of artists on the production of a tremendous atlas. Only once did he leave his work to go out on the roof, when the house in which he was living was showered with enemy incendiary bombs. Then part of the fruit of many years of work was consumed by flames. By the end of 1942 the "Atlas of Nerve and Vein Systems" was completed. The initiator and principal producers of the atlas were duly recognized by the nation and were awarded first class Stalin prizes.

Twenty years ago semiliterate young shoemaker Alexei Maximenkov was working as a medical orderly on the civil war front. There he first came in touch with medicine. After the civil war Maximenkov attended one of the many preparatory schools known as workers' faculties which the Soviet government opened. Ten years later, in 1931, he was graduated from the Academy of War Medicine, of which he now is professor.

Victor Shevkunenko did not select Maximenkov as his pupil and leading assistant by chance. Shevkunenko concluded that the organism of man follows laws discovered by Darwin concerning changing of species. He undertook the task of determining the law of anatomic differences. The atlas contains that part of his observations which is most developed, the greatest possible deviation from normal in structure of the peripheral nervous system and the vein system.

After visiting all main scientific centers in Europe and the United States of America at the expense of the Pirogov stipendium, Maximenkov returned home and for twenty years engaged in surgical and topographic anatomy, at the same time working in the clinic. During this period in the department which he directed, over four hundred and fifty scientific papers appeared; forty professors, fifty lectures and a large number of assistants received diplomas. His researches and those of his students, who numbered some one hundred and fifty persons, finally took a completely new direction in applied anatomy—that of clinical anatomy. The material which Victor Shevkunenko and a large number of doctors collected in the space of thirty-five years was a result of the study of anatomic deviations in the structure of man from Maximenkov's Atlas.

"In wartime," says Alexei Maximenkov, "this material has tremendous significance. In this war the number of limb injuries is extremely great and thousands of doctors every day meet various surprises when treating them."

ORGANIZATION SECTION

OFFICIAL NOTES

DOCTORS AT WAR

Radio broadcasts of Doctors at War by the American Medical Association in cooperation with the National Broadcasting Company and the Medical Department of the United States Army and the United States Navy are on the air each Saturday at 5 p. m. Eastern War Time (4 p. m. Central War Time, 3 p. m. Mountain War Time, 2 p. m. Pacific War Time). An exception is the Chicago area, where the broadcasts are heard by transcription at 10:30 p. m. Saturdays over Station WMAQ.

The titles and guest speakers for the last three programs are as follows:

June 5. "Medical Discoveries in Wartime."
Speaker, Dr. Morris Fishbein, Editor of THE JOURNAL.

June 12. "Doctors for Tomorrow."
Speaker, Brig. Gen. Fred W. Rankin, M. C., A. U. S., President of the American Medical Association.

June 19. "Report to America." See special announcement.

SPECIAL BROADCAST, DOCTORS AT WAR, JUNE 19

The closing program of Doctors at War, scheduled for June 19, will be entitled "Report to America." On this program will appear two Army medical officers broadcasting by short wave from two foreign theaters of war, one Navy officer broadcasting from a foreign theater and one Navy officer broadcasting from a home base. The names of these officers and their locations are not divulged in advance, for military reasons. For the same reason, their subjects will not be announced. We are assured, however, of fresh and timely material arising out of the immediate medical situation in the Army and the Navy. Four doctors actually at war will make a first hand report to America.

This broadcast has been made possible through the generous cooperation of the National Broadcasting Company in arranging the short-wave pickups from foreign advance bases.

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—S. J. Res. 16 has passed the Senate, authorizing an appropriation of $50,000 to construct at St. Lawrence, Newfoundland, a hospital, dispensary or other memorial in token of the appreciation of the United States to the people of St. Lawrence for saving the lives of officers and men of the U. S. S. *Pollux* and the U. S. S. *Truxtun*, wrecked near that community in 1942. H. R. 997 has been reported to the House, proposing to amend the National Defense Act of June 3, 1916 by eliminating the Medical Administrative Corps in the Medical Department of the Regular Army and substituting therefor a Pharmacy Corps. H. R. 2713 has passed the House, making appropriations for the Navy Department and the naval service for the fiscal year ending June 30, 1944. The bill provides that the appropriations for the Naval Establishment may be used for the pay of commissioned medical officers who are graduates of reputable schools of osteopathy.

Bills Introduced.—H. Res. 230, submitted by Representative Kelley, Pennsylvania, proposes to authorize the House Committee on Labor (1) to ascertain by investigation the extent and character of aid now given by the federal, state and local governments and private agencies to the physically handicapped, (2) to investigate the diffusion within the United States of such aid to the physically handicapped and (3) to ascertain the employment opportunities obtaining for the physically handicapped. H. R. 2657, introduced by Representative O'Connor, Montana, provides that, whenever the Secretary of the Interior shall find that the Bureau of Indian Affairs is unable to obtain the services of a sufficient number of physicians and dentists who are citizens of the United States adequately to perform the functions of the bureau with respect to the conservation of the health of Indians, he may, with the approval of the Civil Service Commission, engage the services by contract or otherwise of competent physicians and dentists who are not citizens, for periods of time not to extend beyond the termination of the war and six months thereafter. H. R. 2761, introduced by Representative Andresen, Minnesota, proposes to establish a Civilian Supply Administration with authority, among other things, to ascertain the quantities and types of goods and services, including but not limited to food, clothing, shelter, fuel, transportation and medical care, necessary to keep the civilian population healthy and functioning effectively and to apply to the appropriate government agencies for the amounts and types of manpower, materials, facilities, transportation and other resources determined to be essential to produce and distribute the necessary goods and services.

STATE MEDICAL LEGISLATION

Alabama

Bills Introduced.—S. 41 proposes numerous amendments to the existing law relating to the reporting of births and deaths. Its general purpose is to conform the Alabama law with the vital statistics laws of other states. S. 70 and H. 310 are companion bills and provide for the sexual sterilization of certain inmates who have been committed to hospitals for the insane in the state as a condition to the release or discharge of such inmates; of certain persons who have been lawfully committed to institutions for the treatment of mental defectives or feebleminded; of certain inmates of the state penitentiary who are sexual perverts, sadists, homosexualists, masochists, sodomists or afflicted with any grave form of sexual perversion or constitutionally inferior recidivists; of certain inmates of any reform school, industrial school, or training school or reformatory, and of certain other persons not inmates of any institution who are found by the county board of censors of the county medical society of any county in the state to suffer from a mental deficiency transmissible to offspring. H. 367 proposes to enact a food, drug and cosmetic act.

California

Bills Enacted.—A. J. R. 49, adopted, May 5, memorializes Congress to consider the advisability of making an appropriation to provide funds for paying women in training to become trained nurses a salary during their years of training. A. 326, approved, May 18, amends the existing law relative to the practice of nursing so as to permit the rendering of nursing services by unlicensed persons during a national emergency arising out of war or during an epidemic or other public disaster (chapter 573, Laws of 1943). A. 928, approved, May 15, defines cannabis sativa as the male or female of any species commonly known as cannabis sativa, hemp, Indian hemp or marihuana (chapter 468, Laws of 1943). A. 945, approved, May 13, provides for the issuing of temporary certificates to practice pharmacy valid for

a period of six months (chapter 392, Laws of 1943). A. 1171, approved, May 15, provides for the appointment by the board of medical examiners of one or more committees to determine (1) whether an applicant fulfils all of the requirements for the certificate for which he is applying; (2) where an examination is required, whether the applicant shall be admitted to the examination and the terms and conditions of his admittance and whether he fails or passes; (3) whether a recommendation should be made to the members of the board that the certificate applied for be issued. The purpose of this law is to expedite the granting of licenses to practice medicine (chapter 471, Laws of 1943). A. 1174, approved, May 15, provides a method by which a revoked or suspended license to practice medicine may be reinstated after one year has elapsed from the date of revocation or suspension (chapter 472, Laws of 1943).

Colorado

Bills Enacted.—H. 323, approved, April 22, appropriates to the state board of health the sum of $12,000 for the purchase of a portable photoroentgen (x-ray) unit to be used for the prevention and control of tuberculosis. H. 572, approved, April 28, provides for the establishment and maintenance of public hospitals in counties of the state to be controlled by boards appointed by the county commissioners. Each such board will consist of seven members none of whom may be either a practicing physician or an elective or appointive state, county or city official. The new law provides that every county hospital established under it may accept pay patients.

Connecticut

Bill Introduced.—H. 1383 provides that any graduate of an approved medical school may serve as a resident physician in any state-aided hospital for the duration of the war and for not more than six months thereafter if the written consent and approval of the Connecticut medical examining board has been obtained.

Florida

Bill Enacted.—H. 335, which became a law without the governor's approval, May 12, authorizes the city of Miami to levy an annual tax, not to exceed 4 mills on the dollar, on the real and personal property within the limits of the city for the purpose of maintaining and operating a hospital.

Bill Introduced.—H. 679 proposes to create a board of psychological examiners to examine applicants for licenses to practice psychology defined "as the use and practice of any and all psychological arts, sciences, methods or procedures, now known or hereafter to be known, for the prevention, relief or cure of mental or nervous maladjustments, ailments or diseases, including suggestotherapy, hypnotherapy, psychotherapy, psychoanalysis, and other similar arts, sciences, methods, or procedures."

Illinois

Bill Enacted.—H. 8, approved, May 12, imposes a duty on each county to provide funds for the treatment of persons afflicted with cancer or tumor who are unable to pay for such treatment. If the general funds of the county are insufficient to pay for such treatment, a special tax may be levied and collected for that purpose. The county board of each county will appoint a duly licensed physician to examine applicants for the benefits provided by this law.

Bill Introduced.—S. 468 proposes to amend the Non-Profit Hospital Service Plan Act to provide that before a contract with any subscriber becomes effective, and as a condition precedent, the subscriber must submit to a medical examination before some physician to be designated by the corporation, and a copy of the physician's report must be attached to and become a part of the contract.

Nebraska

Bills Introduced.—Legislative Bill 441 proposes to amend the premarital examination law to provide that no person shall make a charge in excess of 1 dollar for making an examination under the terms of the act. Legislative Bill 442 proposes to amend the prenatal examination law to provide that no person shall make a charge in excess of 1 dollar for an examination made under the law.

Rhode Island

Bill Enacted.—H. 668, approved, April 27, appropriates the sum of $25,000 to be expended under the direction of the state director of health for the hospitalization of wives and children of men in the armed services below the grade of commissioned officer who are unable to pay for such hospital care.

Wisconsin

Bill Enacted.—A. 305, approved, May 18, imposes an annual registration requirement on persons engaged in the practice of medicine and surgery, osteopathy or osteopathy and surgery in the state, registration to be effected in the month of January in each year. The registration fee is to be fixed by the state board of medical examiners for each year but may not exceed $3 in any year. The registration requirement will be inapplicable to any physician while serving in the armed forces of the United States or of an allied government (chapter 155, Laws of 1943).

Bill Introduced.—A. 601 proposes to amend the workmen's compensation act so as to permit chiropractic services to be supplied by an employer in lieu of medical treatment.

MEDICAL ECONOMIC ABSTRACTS

SHAWNEE COUNTY (KAN.) PLAN

Seven months of successful experience with a prepayment plan for dependents on a more comprehensive scale of operation and with several novel features now affords some valuable suggestions to the many state and county medical societies now operating or contemplating the starting of similar plans. Shawnee County, which includes the city of Topeka, has a population of over 90,000.

The agreement between the Shawnee County Medical Society and the Shawnee County Board of Social Welfare and the State Department of Social Welfare provides that "all cases for Old Age Assistance, Aid to Dependent Children and General Assistance may receive the benefits of medical care, if they choose to do so by the payment of $3 per month. These payments for General Assistance cases are made directly by the welfare agencies either monthly or at six months intervals in advance." [1]

It was mutually agreed that all assistance cases, persons or patients affected shall have a free choice of physicians participating.

The county medical society agrees to furnish ordinary and reasonable medical and surgical care compatible with the standards and ethics established by the profession and within the ability and scope of the participating physicians and within the customary and usual practice of the physicians whereby the well being of patients is assured by providing them with the best possible medical care including ordinary and reasonable hospitalization, drugs and medicines, and specialized services when such are approved by the county medical society and when such drugs and medicines are included in a prescription issued to patients by participating attending physicians. It is understood, however, that the services include only those which are deemed to be essential to the needs and welfare of patients and which are approved by the county medical society.

The following services are not included: surgery and treatment not within the customary and usual practice of the participating physicians; surgery and treatment for which necessary equipment, facilities or incidentals are not available or provided; dentistry, nursing; appliances including eye glasses, and services available through other agencies.

Careful preparation preceded the inauguration of the plan. All members of the county medical society were questioned as

1. J. Kansas M. Soc. **43**: 483, 491 (Dec.) 1942.

to willingness to cooperate and the capacity in which they wished to serve.

On the basis of the replies to the questionnaire, 28 members were assigned to home call service, 40 to the clinic staff and 11 for specialized services in their offices or at hospitals. The Shawnee County Medical Society was particularly fortunate at this step of the organization, as the city of Topeka turned over to the society all the facilities in its new modern and moderately equipped city clinic rooms. With these facilities the society was able to set up fourteen specialized clinics in addition to the general medical clinic which is held daily, each doctor serving an average of two hours each week. In addition to the medical clinic, the following clinics are now in operation: surgery, gynecology, eye, ear, nose and throat, pediatrics, proctology, tuberculosis, child welfare, diabetic, neuropsychiatry, antepartum, dermatology, urology, cardiology and venereal disease. When surgical operation is required, the patient may also choose any surgeon in the society to do what is necessary. A druggist is employed by the society at the clinic to fill the prescriptions during clinic hours. Emergency prescriptions are either filled by the druggist or supplied by the attending physician from a kit issued by the dispensary. The average number of prescriptions issued in a month is around eighteen hundred.

MEDICAL PLANNING IN SOUTH AFRICA

The Federal Council of the South African Medical Association at its meeting on April 26, 1941 appointed a planning committee to study and prepare proposals regarding the organization of medical care.[1] This committee considered its task to be:

(*a*) Pointing out clearly the defects of present day services.
(*b*) Stating what should be aimed at in an ideal service.
(*c*) Describing the various practical methods that might be adopted to arrive at this ideal.
(*d*) Attempting to arrive at unanimity in the profession in recommending the adoption of some particular scheme for the improvement of health services and to do everything possible to press for such a scheme being put into operation by the government.

The association had previously adopted a resolution to support a national health insurance scheme if introduced by the government, but, when the committee conducted a referendum to determine whether this action still represented the opinion of the medical profession, a vote of 413 to 95 was registered against the support of the resolution.

As a first step the members of the association were urged to suggest plans and express themselves fully concerning the most desirable action to be taken. There was an extensive response, so that "articles on planning have appeared in practically every number of THE JOURNAL since that of the 10th of May 1941." A wide variety of proposals for plans were received, several of which were endorsed after discussion by one or more divisions of the association.

As the next step the committee classified these plans as far as possible and has now asked for another referendum to determine the attitude of the medical profession and afford a guide toward action. In the first referendum about 10 per cent were in favor of the present system, or the maintenance of the status quo. The plans of those who desired some change fell into two classes: "(*a*) Those retaining private practice as an integral part of the health services. (*b*) Completely socialized health services. Private practice would not be prohibited but would not be an integral part of the scheme."

The first question asks the physicians to state which of these two classes of plans is preferred. A brief sketch of each of the proposals is then given with opportunity to indicate a choice of modifications of some of the plans. Altogether a yes or no vote is requested on twenty-three questions indicating a preference for a correspondingly wide choice of proposals. It is hoped in this way to obtain a fairly accurate picture of the attitude of the profession, on a wide variety of proposals which will form a basis for further action.

The proposals to be voted on cover a wide field. The multiple benefit society, a form of contract practice, "is rapidly expanding and it has recently received official government encouragement." An earlier vote "indicated a certain amount of support for this type of practice, but, on the other hand, there were more votes against it than for any of the other forms of organized service suggested." National health insurance is regarded by a "fair number of practitioners" as a "logical first step to be taken in the direction of an organized medical service," although "nowhere does there seem to be anything like complete satisfaction with it either on the part of the profession or the public."

There are a number of plans that are classified as "socialized medicine," since "private competitive practice is not contemplated as an integral part of any of them," although it will not be "forbidden or even discouraged." All such plans contemplate "(*a*) Cutting at the roots of ill health by drastic reforms in such fields as nutrition, housing, physical education, rehabilitation and social security generally. (*b*) Unified control of all health activities. (*c*) State finance and cooperation with other state departments. (*d*) Representation of medicine and allied professions in administration and control. (*e*) Health education. (*f*) Health conservation."

1. A Health Service for South Africa, South African M. J. **16**: 425 (Dec. 26) 1942.

WOMAN'S AUXILIARY

New Jersey

A joint meeting of the Contemporary Club of Newark and of the Woman's Auxiliary to the Essex County Medical Society was repeated by request on January 26. Invitations were sent to all social organizations, public health and welfare agencies, as well as hospital representatives and nurses. The speakers were introduced by Dr. William W. Cox, president of the Essex County Medical Society. Lieutenant Jean Robb of the Woman's Auxiliary Army Corps spoke on the purpose of the Waacs. Dr. J. Wallace Hurff talked on "Medicine in War" from the civilian doctor's point of view. Dr. Stuart Z. Hawkes spoke on "Medicine in War" from the military angle.

Mrs. Max Kummel, chairman of public relations of the auxiliary, and Mrs. Frank A. Bien were the joint chairmen of this program.

Pennsylvania

A meeting of the Allegheny auxiliary in Pittsburgh recently was called to order by the president, Mrs. Robert C. Hibbs, who announced that $1,700 had been turned over to the Student Loan Fund by the auxiliary. This fund, which has been in existence for twelve years, was organized for the benefit of needy medical students of the University of Pittsburgh. Early in the year a request was made by the university. The auxiliary was happy to respond with the amount stated, which is the largest ever given by the auxiliary since the fund was started.

The food mart, under the chairmanship of Mrs. N. Park Davis with Mrs. Henry D. Jorden as co-chairman, proved a great success. The cakes, pies, cookies, rolls, preserves and jellies were donated. Members also contributed handwork. The proceeds, nearly $470, will go to the Student Loan Fund.

West Virginia

At the nineteenth annual meeting of the Woman's Auxiliary to the West Virginia State Medical Association at Charleston, May 17 and 18, Mrs. John P. Helmick of Fairmont was installed as president, succeeding Mrs. Ralph Hogshead of Mammoth. Other officers installed were Mrs. H. P. Evans of Keystone, Mrs. W. E. Hoffman of Charleston, Mrs. N. L. Haislip of Wheeling and Mrs. H. D. Gunning of Ronceverte as vice presidents, Mrs. J. W. Carney, Logan, recording secretary, and Mrs. S. W. Davis, Fairmont, corresponding secretary. Mrs. Scott A. Ford, Edwight, is the president-elect and will take office at the annual meeting in 1944.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

CALIFORNIA

Dr. Soiland Honored.—The Radiological Section of the Los Angeles County Medical Association gave a dinner, May 5, in honor of Capt. Albert Soiland (MC), U.S.N.R., celebrating his seventieth birthday. In 1933 the sixtieth birthday of Dr. Soiland was celebrated by the dedication to him of the May issue of *Radiology*. A founder of the American College of Radiology, serving as its president in 1931, he was also a sponsor of the plan to establish the Section on Radiology of the American Medical Association and in 1926 was elected its chairman.

University Appointments.—Dr. Ernest D. Gardner, instructor in anatomy at Stanford University School of Medicine, San Francisco, has been appointed assistant professor of anatomy at the University of Southern California School of Medicine, Los Angeles, and Dr. Arnold Lazarow of the department of anatomy, University of Chicago School of Medicine, has been named research assistant in the department of anatomy at Southern California. Dr. Jurgen Ruesch of Zurich and Basel has been appointed lecturer in psychiatry at the University of California Medical School, San Francisco. Since the outbreak of the war he has held a Rockefeller Foundation fellowship and has been working in Boston hospitals and at the Harvard Medical School, Boston, *Science* reports.

ILLINOIS

New Reportable Diseases.—Effective on May 15 the following have been added to the list of reportable diseases in Illinois: rheumatic fever, hemorrhagic jaundice (Spirochetosis icterohemorrhagica, Weil's disease), infectious hepatitis (acute catarrhal jaundice), infectious keratoconjunctivitis (superficial punctate keratitis, nummular keratitis).

Chicago

Dr. George Gardner Named Assistant Dean at Northwestern.—Dr. George H. Gardner, associate professor of gynecology at Northwestern University Medical School, has been appointed assistant dean and Dr. Alexander A. Day has been named acting assistant dean in place of Lieut. Col. Harold A. Davenport, M. C., A. U. S. Dr. Gardner graduated at Johns Hopkins University School of Medicine, Baltimore, in 1921, serving there on the faculty until 1926, when he joined the staff at Northwestern as clinical assistant in gynecology. He is president-elect of the Chicago Gynecological Society.

The Ricketts Prize.—The Howard Taylor Ricketts Prize of the University of Chicago has been divided between Dr. Howard C. Hopps, instructor in pathology, and Leo R. Melcher, Ph.D., formerly assistant in immunology in the department of bacteriology and parasitology and now a student at Northwestern University Medical School. Dr. Hopps's research showed that although some allergy-causing substances may hinder the healing of wounds if they are used in treatment, catgut, used in wound repairs and often suspected of having this effect, actually is not responsible. Dr. Melcher's work concerned the analysis of the substances in the worm Trichina which cause immunity in the disease of trichinosis. Dr. Hopps graduated at the University of Oklahoma School of Medicine, Oklahoma City, in 1937 and two years later joined the department of pathology at the University of Chicago. Dr. Melcher graduated at the University of Chicago in 1939 and received his Ph.D. in 1942.

Michael Reese Hospital Launches Program of Medical Teaching.—The Michael Reese Hospital has inaugurated a program of medical teaching which is to be developed first on an intramural basis but which will gradually be merged into postgraduate teaching available to the medical profession at large. It is hoped that the program will be sufficiently advanced by the end of the war to help meet the demand for refresher courses for physicians now in the armed forces. The part time and full time staffs of the clinical departments of the hospital, and the full time staffs of the Research Institute and of the clinical laboratories will all contribute to the teaching faculty. In line with the introduction of the new teaching program and as a part of the general reorganization at the hospital Dr. Herman Smith, who has been the general superintendent of the hospital, now becomes the executive director and Dr. Samuel Soskin, head of the department of metabolism and endocrinology at Michael Reese for the past fourteen years, has been appointed medical director and dean of the new teaching and research faculty.

IOWA

Radio Program on Child Development.—The seventeenth Iowa Conference on Child Development and Parent Education will be conducted by radio on June 15 in line with the national effort to reduce civilian travel. "Today's Children Tomorrow" will be the theme of the conference, which is held annually under the auspices of the Iowa State Council for Child Study and Parent Education in cooperation with the Iowa Child Welfare Research Station, Iowa City, and the extension divisions of the State University of Iowa, Iowa City, Iowa State College of the Agriculture and Mechanic Arts, Ames, and State Teachers College, Cedar Falls. Among the speakers will be Robert R. Sears, Ph.D., Iowa City, on "Shall We Neglect Our Children?" and William F. Ogburn, Ph.D., Chicago, "The Child in the Future."

MAINE

State Medical Meeting.—The house of delegates of the Maine Medical Association will meet at the Augusta House, Augusta, June 20. Dr. Oscar F. Larson, Machias, council chairman, will preside at the first session in the absence of Dr. Stephen A. Cobb, Sanford, president-elect, now in military service. Dr. Carl H. Stevens, Belfast, president of the association, will preside at the luncheon meeting, at which Andre William Reggio, surgeon (R), U. S. Public Health Service, regional medical officer, First Civilian Defense Region, Boston, will discuss "Emergency Medical Service—Office of Civilian Defense." A second meeting of the house of delegates will conclude the one day session.

MASSACHUSETTS

Changes in Status of Licensure.—At a meeting of the state board of registration in medicine, April 14, it was voted to restore the license to practice medicine in the commonwealth of Dr. Daniel E. Nyman, Arlington. The board also voted to revoke the license of Dr. Solomon P. Bialow, Waltham, because of gross misconduct in the practice of his profession as shown by his conviction in court.

Tufts Building Fund Now $500,000.—A new gift of $47,800 from Dr. and Mrs. George G. Averill, Waterville, Maine, brings the building fund at Tufts College Medical School, Boston, up to $577,000. Dr. Averill graduated at Tufts in 1896. The recent gift brings his total contributions to the building fund up to $100,000. During 1942, $50,000 was raised for the building fund and $54,000 was received from individuals, foundations and other sources for teaching, research and scholarships.

New State Health Commissioner.—Dr. Vlado A. Getting, since 1942 commissioner of health of Worcester, has been appointed commissioner of public health of Massachusetts to succeed Dr. Paul J. Jakmauh, Boston. Dr. Getting graduated at Harvard Medical School, Boston, in 1935 and subsequently received the degrees of master of public health and doctor of public health from Harvard University. After interning at the Worcester City Hospital, he became associated with the state department of public health, first as assistant epidemiologist, then as director of a mosquito survey and last as a district health officer. Dr. Getting was forced to resign from the medical corps reserve of the U. S. Army in 1942 because of a physical disability.

MICHIGAN

State Health Officer Reappointed.—Dr. Henry Allen Moyer, Lansing, has been reappointed state health commissioner for a four year term beginning June 30.

First Nursery Schools Open.—The Detroit Board of Education on May 7 opened sixteen nursery schools for children from 2 through 5 years of age, the first to be established with federal Lanham funds. Plans provide for the establishment of fifty such centers in Detroit.

State Increases Funds for Hospital Care.—The state department of health announces that additional state funds will be available July 1 to aid Michigan counties in providing hospital care for persons who have tuberculosis. The legislature has provided $2,900,000 to cover the state's share of the cost of hospital care for patients who are county charges during the next fiscal year, or $750,000 more than the current appropriation. A half million dollars is expected to cover the increase from $1.50 to $2 per patient day in the hospital in state pay-

ments to counties voted during the recent session. A separate $250,000 item is for increased assistance to counties whose tax incomes are too small to cover their share of the cost of hospital care for their tuberculous charges.

Wayne County Health Department Created.—On April 21 the board of supervisors of Wayne County established a Wayne County Department of Health. Members of the board of health include Drs. Lloyd K. Babcock, Detroit (three year term), and John W. Nagle, Wyandotte (two year term). Other members of the board are Charles E. Brake, deputy superintendent of schools (five year term), George Boik, clerk of Taylor Township (one year term) and Joseph H. McCann, postgraduate student in public health at the University of Michigan (four year term). The establishment of the department followed a health survey largely supervised by the Wayne County Board of Auditors, of which Dr. Paul A. Klebba, Detroit, is medical adviser. In addition to the five member board which will direct the department there will be a director, a deputy health officer, one sanitarian, one supervising nurse, four nurses, one statistical clerk-stenographer and one laboratory technician.

University Cooperates with Foundation on Infantile Paralysis Study.—The National Foundation for Infantile Paralysis and the University of Michigan have joined in a long-range program for the training of doctors, public health workers and laboratory technicians to study infantile paralysis and other virus diseases. The program, which has been developing for three years, will be expanded to its full scope by June 1, when the university opens its new three story School of Public Health at Ann Arbor. The new structure will house a unit devoted entirely to work in virus diseases, particularly infantile paralysis. The virologists who will be trained under the program will be prepared to attack the whole realm of virus diseases, including not only infantile paralysis but also influenza, atypical pneumonias, St. Louis and equine encephalitis, measles, chickenpox, smallpox and mumps. To aid in the necessary planning and execution of the project the National Foundation has made a three year grant, totaling $120,000, to the university in addition to three previous grants, totaling $110,000, made in the past three years. According to a release from the foundation, this is the first time in the history of the foundation that three long-term grants have been made within the space of a single year. Recently a five year grant of $150,000 was made to Yale University, New Haven, Conn., to establish the Yale Poliomyelitis Study Unit, and in 1942 $300,000 was given to Johns Hopkins University, Baltimore, under a five year grant to establish and conduct the Center for the Study of Infantile Paralysis and Related Virus Diseases.

MINNESOTA

Dr. Snyder Gives the Dight Institute Lecture.—Laurence H. Snyder, Sc.D., chairman of the department of zoology, Ohio State University, Columbus, delivered the second annual lecture under the Charles Fremont Dight Institute for the Promotion of Human Genetics on "Heredity and Modern Life," April 19. The institute was established in 1942 (THE JOURNAL, June 13, 1942, p. 572) under the will of Dr. Charles Fremont Dight, who had been a member of the staff of the University of Minnesota Medical School, Minneapolis. The income of a fund of more than $100,000 was bequeathed to the university to endow the institute, and studies were to be directed particularly to "a search for traits, such as metabolic disturbances, which may have genetic bases but are not recognized as hereditary traits."

MISSOURI

Virus Diagnostic Service.—The laboratory section of the St. Louis Health Division has established a virus diagnostic unit for physicians wishing laboratory assistance in the diagnosis of virus diseases. At present the service is limited to the neurotropic virus diseases.

Personal.—Dorothy A. Hehmann has resigned as executive director of the Missouri state cancer commission to become personal director of the New Haven Hospital, New Haven, Conn.——Dr. John I. Byrne, St. Joseph, has been appointed a member of the board of health, succeeding Dr. Leon Paul Forgrave, St. Joseph, resigned.

Annual Loeb Lecture.—Col. Richard P. Strong, M. C., A. U. S., gave the eighth annual Leo Loeb Lecture at the Washington University School of Medicine, St. Louis, April 29. His subject was "The Importance of Tropical Diseases in Relation to the Present War." The lecture is sponsored by the Mu chapter of Phi Beta Pi in honor of Dr. Leo Loeb, St. Louis, who in 1936, when the lectureship was established, was professor of pathology at the medical school. Dr. Loeb has been professor emeritus since 1937.

NEW JERSEY

New Medical Fund.—Announcement has been made of a recently accumulated fund in the Newark Beth Israel Hospital Research Foundation in honor of the memory of Mrs. Dorothea Lichtman, wife of the president of the foundation, Abraham Lichtman. The foundation was formed in 1941 and is a corporation separate from the hospital organization but embracing what was then known as the institution's division of laboratories. It is supported by donations and by members of the hospital staff who carry on independent research.

NEW YORK

Aid for Adult Poliomyelitis Cases.—*Health News* reports that an appropriation of $20,000 has been made in the state budget for the coming fiscal year to provide state aid for such remedial care of adult poliomyelitis cases as may be authorized by local boards of health and health officers and approved by the state commissioner of health. Inquiries regarding procedures for making application for care under the provisions of this legislation should be directed to the district health officer.

Honorary Degrees Conferred.—At its annual commencement, May 2, the University of Rochester, Rochester, conferred the honorary degree of doctor of science on Sister Elizabeth Kenny for her work in treating infantile paralysis. Similar degrees were conferred on Dr. Stanhope Bayne-Jones, professor of bacteriology at Yale University School of Medicine, New Haven, Conn., on leave as a colonel in the army medical corps, and Roger Adams, Ph.D., head of the chemistry department at the University of Illinois, Urbana, Ill., and one of the five chemists in charge of the nation's chemical warfare research.

Cancer Teaching Day.—June 17 will be the occasion of the cancer teaching day at the Hotel Utica, Utica, under the auspices of the Medical Society of the County of Oneida, Utica Academy of Medicine, state medical society and its fifth district branch, and the state department of health. "The Management of the Patient with Advanced Cancer" will be discussed by Dr. Norman Treves, New York, and "Cancer of the Larynx, Bronchi and Esophagus" by Dr. Chevalier L. Jackson, Philadelphia. An evening meeting will be addressed by Drs. George E. Binkley and Lloyd F. Craver, New York, on "Cancer of the Colon and Rectum" and "The Significance of Enlarged Lymph Nodes" respectively.

Industrial X-Ray Laboratory.—An industrial x-ray laboratory equipped with a million volt unit, a joint enterprise of the University of Rochester and eight industries, was formally opened on April 19. Ernest E. Charlton, Ph.D., of the General Electric Research Laboratories, Schenectady, who designed the apparatus, said in an address that the project represents "a novel and most useful cooperation in the joining of hands of university and industry in the developing of the full use of x-rays in the industrial field." The undertaking was financed by the Eastman Kodak Company, Rochester Products and Delco Appliance divisions of General Motors, the Pfaudler Company, the Rochester Gas and Electric Corporation, Consolidated Machine Tool Corporation, Symington-Gould Company and the Rochester Brewing Company. According to *Science* the university supplies the scientific staff to make the tests and is free to use the equipment for research in metallurgy, medicine and engineering. Part of a second million volt unit is installed in another part of the laboratory for medical research on cancer. The remainder will not be available until after the war, it was stated.

New York City

Fraternity Sells $600,000 in War Bonds.—A luncheon celebration will be held at the Waldorf Astoria Hotel, June 5, at which treasury department officials will name two heavy bomber planes in honor of the Phi Delta Epsilon Medical Fraternity, which sold $600,000 in war bonds during the last drive.

The Adam Miller Lecture.—Dr. Carl J. Wiggers, professor and head of the department of physiology, Western Reserve University School of Medicine, Cleveland, recently delivered the Adam Miller Lecture at Long Island College of Medicine, Brooklyn, on "Recent Experimental Approaches to the Shock Problem."

Funds for Child Care.—About $20,000 in state funds has been allocated to finance the child care activities of twenty-eight New York City settlement houses. The twenty-eight centers have applied for regular participation in the state war

council's child care program. An emergency authorization has been granted for two months and a permanent arrangement will be made after the city's new fiscal year begins, July 1.

Funds for Nursery Care.—The Board of Estimate voted on April 22 to provide city funds, estimated at about $120,000 a year, to aid in paying for day nursery care of children of working mothers. The board acted under state legislation stipulating that the state will pay one third of the cost, the city one third and the mothers one third. The state legislature had appropriated $2,500,000 for state aid in connection with wartime child care projects.

First Prize in Cancer Exhibit.—"The Cure of Cancer is the Duty of Society" was the theme of the first prize winning exhibit in the competition conducted in the city's schools by the New York City Cancer Committee of the American Society for the Control of Cancer. Eight boys and girls, students of the Forest Hills High School, formed the prize winning team for the exhibit, which portrayed some of the significant contributions made by laboratory investigations on mice and rats.

Refresher Course in Venereal Diseases.—A clinical refresher course in the modern diagnosis and management of venereal diseases opened, May 12, at the Central Clinic of the city department of health, 130 Leonard Street, Manhattan, under the auspices of the bureau of social hygiene. Dr. Louis Chargin, consultant to the bureau, will direct the course, which will be held each Wednesday morning through June 30. The course offers practitioners the opportunity to observe laboratory and clinical diagnostic procedures and treatment methods for syphilis, gonorrhea, chancroid and other venereal diseases.

Physician Sentenced for Income Tax Evasion.—According to the New York *Times*, Dr. Mandel Frankel was given a prison term of a year and a day, April 19, for evasion of income taxes amounting to more than $36,000 for the years 1928 to 1938. The *Times* reported that the physician, said to be the operator of a large farm at Mount Bethel, Pa., pleaded guilty to the charges last January. The newspaper further reported that Dr. Frankel was said by the government to have derived part of his income from an "abortion mill" at 241 East 18th Street. He was allowed until April 29 to begin serving his sentence.

Dr. Bolduan to Retire June 1.—Dr. Charles F. Bolduan, organizer and first director of the bureau of health education of the city department of health, will retire on June 1. At a dinner to mark his retirement, held on May 20, the speakers included Dr. James Alexander Miller, Edward H. Lewinski-Corwin, Ph.D., and Dr. Haven Emerson. Dr. Bolduan, who reached the civil service age limit of 70 years on May 7, began his association with the department of health in 1904, when he was appointed bacteriologist. In 1907 he became assistant to the late Dr. Hermann N. Biggs, who was then general medical officer of the department. Six years later Dr. Bolduan established the bureau of health education. For the interim 1918-1928 he served with the U. S. Public Health Service. He formerly was professor of bacteriology at Fordham University School of Medicine (now extinct) and lecturer on preventive medicine and public health at Columbia University College of Physicians and Surgeons.

OHIO

Memorial to Dr. Crile.—The *Cleveland Clinic Quarterly* has dedicated its April issue to the memory of the late Dr. George Crile, a founder and former president of the Cleveland Clinic Foundation. The *Quarterly* carries the addresses that were presented at the memorial service for Dr. Crile at Western Reserve University on January 24.

New Venereal Disease Control Officer.—Roger E. Heering, passed assistant surgeon, U. S. Public Health Service, has been lent to the state for service as venereal disease control officer. Dr. Heering came from district number 1, U. S. Public Health Service, with headquarters in New York, where he had been venereal disease consultant for ten states included in the district. Dr. Heering had been lent to Ohio during the period 1939-1940 as venereal disease control officer in the Cincinnati area.

Retires as Secretary After Forty-Three Years.—Dr. Oliver T. Sproull, West Union, secretary of the Adams County Medical Society since 1900, declined reelection this year. Dr. Adams was a charter member of the society when it was organized in 1886. He has practiced in the county ever since he graduated at the College of Physicians and Surgeons, Baltimore, in 1886. His successor as secretary of the society is his daughter, Dr. Hazel L. Sproull, associated with him in practice at West Union.

PENNSYLVANIA

Personal.—Dr. Thomas H. A. Stites has resigned as medical director of the Pennsylvania State Tuberculosis Sanatorium number 2 at Cresson, concluding twenty-nine years service to the state, sixteen of which have been spent at the Cresson Sanatorium. Dr. Stites plans to live at Nazareth.——Dr. Augustus H. Clagett, Upper Darby, has resigned as secretary of the Delaware County Medical Society to take up residence in Ocean City, N. J.; he is retiring from active practice. Dr. Richmond C. Holcomb, Upper Darby, will act as secretary for the unexpired term.

Philadelphia

Department of Health Resumes Bulletin.—The Philadelphia Department of Health has resumed publication of a bimonthly *Health Bulletin* which was discontinued in 1941 because of insufficient funds. This year Mayor Samuel approved a sum granted by the city council to publish again the bulletin and other health reports.

HAWAII

Medical Society Commended for Prewar Services.—A senate resolution was adopted on April 26 in the legislature of the Territory of Hawaii "proclaiming and recording the outstanding service by the Honolulu County Medical Society and the physicians and surgeons volunteering for service on Dec. 7, 1941 in the care of the wounded of the armed forces." The resolution points out that the Honolulu County Medical Society had its prewar services so well organized that the members of the profession were able to perform "swiftly and efficiently the extraordinary tasks they were called on to do in caring for the casualties among the members of our armed forces." In recognition of the outstanding service, the senate adopted the resolution.

Hospital for Paralysis Patients.—The Office of Civilian Defense has erected a wooden building on the grounds of the Shriners' Hospital for Crippled Children, Honolulu, as emergency quarters for patients with poliomyelitis, following an outbreak which was first reported in February. Newspapers report that since February 34 cases have been placed under treatment. The outbreak is said to be confined to congested areas of Honolulu and is not an epidemic. Seven adults are included among the patients. Lieut. Gen. Delos C. Emmons, commanding the Hawaiian Department of the U. S. Army, has contributed $5,000 to the emergency infantile paralysis hospital from the army's community chest fund. Brig. Gen. Edgar King, U. S. Army, department surgeon, furnished the material and army nurses for the hospital, which is staffed by civilian physicians.

GENERAL

Theobald Smith Award to Be Continued.—The original gift from Eli Lilly and Company to the American Association for the Advancement of Science for the Theobald Smith Award was for a period of five years. The grant expired this year with the award to Dr. Sidney C. Madden, New York (THE JOURNAL, May 1, p. 51). The interest in the award, which consists of $1,000 and a bronze medal, has been so great and the researches by young scientists for which it has been given have been of such a high order of merit that Eli Lilly and Company have notified the association of their intention to continue the award for at least three years.

Memorial to Dr. William P. Wherry.—The establishment of a memorial to the late Dr. William P. Wherry, Omaha, for many years secretary-treasurer of the American Academy of Ophthalmology and Otolaryngology, has been authorized by the council of the academy. The memorial, which is to be financed by the interest on $16,000 to be raised by voluntary subscription and invested in war bonds, is to be in the form of a paid-up membership in the academy to the person selected annually by the American Board of Otolaryngology as the most outstanding candidate examined. According to the *Transactions* of the academy, only one half of the objective has been subscribed.

Field Service to Aid Acceleration of Basic Nursing Education.—To help schools of nursing plan acceleration of basic nursing education programs, the National Nursing Council for War Service has been granted a fund for field service by the W. K. Kellogg Foundation. The program of field consultation was to begin in April in the states requesting it and extend up to the time of the National League of Nursing Education's annual meeting in June. The director of the field service is Helen G. Schwarz, R.N., who is on a leave of

absence from her position as dean of the College of Nursing and Health of the University of Cincinnati and director of nursing in the Cincinnati General Hospital.

New Tuberculosis Research.—A new tuberculosis research program has been initiated under the direction of Passed Assistant Surgeons Carroll E. Palmer and Herman E. Hilleboe of the U. S. Public Health Service, with assistance from the National Tuberculosis Association. Student nurses in general hospitals will be the subjects for the study, which aims to discover the constitutional factors that decide whether or not a person will be able to resist the tuberculosis germ invasion, according to *Victor News*. Student nurses were selected for the study because they are subjected to frequent contact with active cases of tuberculosis and can be examined at short intervals during their three year period of training.

Wartime Conference for Libraries Association.—"Information for Victory" will be the theme underlying the several sessions of the 1943 Wartime Conference of the Special Libraries Association which will be held, June 22-24, in New York at the Hotel Pennsylvania. Members of the Special Libraries Association, a national organization with eighteen chapters in the United States and two in Canada, are information specialists in advertising agencies, banks, chemical firms, engineering companies, insurance companies, government agencies, museums, newspapers, religious institutions, in short, in virtually every field of knowledge. Miss Marguerite Burnett is chairman of the Wartime Conference Committee and librarian of the Federal Reserve Bank of New York.

Meeting of Genitourinary Surgeons.—The fifty-fifth annual meeting of the American Association of Genito-Urinary Surgeons will be held at the Red Lion Inn, Stockbridge, Mass., June 10-12, under the presidency of Dr. Nathaniel P. Rathbun, Brooklyn. Among the speakers will be:

Dr. Vincent A. Balkus, Philadelphia, Extraction of Ureteral Stones: Presentation of a New Instrument.
Drs. Alexander R. Stevens and Victor F. Marshall, New York, Methods of Reimplantation of the Ureter into the Bladder.
Drs. Rathbun and Heinrich L. Wehrbein, Brooklyn, Lymphosarcoma of the Bladder: Review of the Literature and Case Report.
Drs. John K. Ormond and Russell B. Roth, Detroit, Recent Cases Illustrating Dangers and Failures of Sulfa Drugs.
Drs. Reed M. Nesbit and Edgar A. Webb, Ann Arbor, Mich., Evaluation of the Pituitrin Concentration Test of Renal Function.
Dr. Hugh H. Young, Baltimore, Surgical Treatment of Elephantiasis.

Dr. du Vigneaud Receives Mead Johnson Award.—The $1,000 award given each year by Mead Johnson & Co. for researches on the B complex vitamins has been awarded this year to Vincent du Vigneaud, Ph.D., professor of biochemistry, Cornell University Medical College, New York, for his work on the structure of biotin. The recipient of the award is chosen by a committee of judges of the American Institute of Nutrition, and the award ordinarily is announced at the institute's annual meeting. The meeting was canceled this year because of the war. Associated with Dr. du Vigneaud in the two year research leading to the elucidation of the chemical structure of the formula of biotin announced last year are the following, all of whom hold the degree of doctor of philosophy: Klaus Hofmann, Donald B. Melville, Glen W. Kilmer, George B. Brown, A. W. Moyer, Julian R. Rachele, Marvin D. Armstrong, all of Cornell, and Hugh H. Darby of Columbia, Karl Folkers, Donald E. Wolf, Ralph Mozingo, John C. Keresztesy and Stanton A. Harris, all of the Research Laboratories of Merck & Co., Inc., Rahway, N. J.

Annual Meeting of Tuberculosis Physicians.—The annual meeting of the American Academy of Tuberculosis Physicians will be held at the Palmer House, Chicago, June 9-10, under the presidency of Dr. Karl J. Henrichsen, Chicago. Among the speakers will be:

Dr. Jacob W. Cutler, Philadelphia, Advanced Tuberculosis and Pregnancy as Influenced by Collapse Therapy.
Dr. Charles F. Taylor, Norton, Kan., Emphysema—Treatment.
Dr. Maurice A. Pollock, Toronto, Bronchiectasis.
Dr. Harry J. Corper and Maurice L. Cohn, Ph.D., Denver, Specific Tuberculosis Immunity During Infection.
Dr. Arthur H. Beebe, Stillman Valley, Ill., Tuberculosis: Common Sense Angle—Forty Year View.
Dr. Laurie Lee Allen, Milwaukee, Nontuberculous Lesions of the Lungs.
Dr. David Salkin, Hopemont, W. Va., Treatment of Tuberculous Bronchitis.
Dr. Leroy Elrick, Denver, Coexistence of Pulmonary Tuberculosis and Mitral Stenosis: Report of Case with Autopsy Findings.
Dr. Giles Wolverton, Dayton, Ohio, Body Section Radiography: Its Practice Value in Pulmonary Tuberculosis.
Dr. William F. Petersen, Chicago (subject not announced).
Lieut. Comdr. Oscar S. Levin, Denver, U. S. Navy, retired, Tuberculology—the Science of Tuberculosis; The Medical Tuberculologist—A Specialist in the Science of Tuberculosis.

Dr. Zoltan Galambos, Chicago, will address the luncheon session Wednesday on "The Tuberculosis Specialist in Undergraduate, Graduate and Postgraduate Medical Education."

Government Services

Information Concerning Drugs That Should Be Sold Only To or On the Prescription of Physicians, Dentists or Veterinarians

The Food and Drug Administration has received numerous requests from drug manufacturers, retail and wholesale drug associations and others for a list of those drug products which it considers dangerous when sold otherwise than on the prescription of a physician, dentist or veterinarian licensed by law to administer drugs.

In answer to such requests, the administration has pointed out that the Food, Drug and Cosmetic Act places on the manufacturer and the distributor the responsibility for properly safeguarding the marketing of drugs which may be dangerous to the purchaser if distributed without restriction. Obviously it is impossible to list all drugs which may be dangerous, since not only the compositions but also the directions for use and the conditions in which their use is recommended may have a very definite bearing on the question of safety or danger. As examples of drugs which are considered dangerous when distributed for use otherwise than on prescription, the following have been mentioned:

Aconite
Aminopyrine
Barbiturates
Benzedrine sulfate (for internal use)
Cantharides (for internal use)
Chrysarobin or goa powder
Chrysophanic acid
Cinchophen, neocinchophen and other cinchophen derivatives
Colchicine
Colchicum
Emetine
Phosphides
Phosphorus
Radium
Sulfanilamide
Sulfapyridine
Sulfathiazole
Tansy, tansy oil
Thiocyanates
Thyroid

The anthelmintic drugs:
- Carbon tetrachloride
- Tetrachlorethylene
- Male fern (aspidium)
- Santonin
- Wormseed oil (chenopodium oil)
- Thymol

It is the opinion that preparations containing bromides should not be sold without prescription if the dosage provided involves the consumption of more than 30 grains per day or more than 15 grains during any three hour period.

The same is true of acetanilid, in the case of medicines that provide a total daily intake of more than 5 grains or more than 2½ grains during any three hour period.

For bromide-acetanilid combinations it has been suggested that preparations for lay use should not provide more than a total daily dose of 15 grains of sodium bromide and 5 grains of acetanilid, or more than 7½ grains of sodium bromide and 2½ grains of acetanilid during any three hour period. Comparable amounts of other bromide preparations should, of course, be subjected to the same restrictions.

There is ample scientific evidence to support the view that preparations providing a daily dose of more than 15 grains of acetophenetidin or more than 15 grains of antipyrine are dangerous within the meaning of section 502(j) when distributed for indiscriminate lay use. Investigations which are currently in progress strongly suggest the probability that somewhat smaller daily doses of these drugs may likewise be dangerous when consumed indiscriminately. After public notice the regulatory program will, of course, include actions based on sales of acetophenetidin and antipyrine under circumstances providing for a somewhat smaller daily dose if scientific opinion becomes available to establish the illegality of such sales.

In the judgment of the Food and Drug Administration epinephrine in solution of 1 per cent or stronger cannot safely be indiscriminately used, and the same is true of ipecac in daily dosage greater than 10 grains, as well as of strychnine in a daily dose greater than 1/20 grain.

It has also expressed the opinion that products containing therapeutically effective proportions of digitalis, squill, strophanthus or other pharmacologically related drugs may not be safe for indiscriminate distribution.

It has been found that manufacturers of such drugs as have been mentioned have taken advantage of the regulation permitting omission of directions for use and substitution of the so-called "prescription legend." Where the legend "Caution: To be used only by or on the prescription of a Physician (Dentist or Veterinarian)" appears on the package in lieu of directions for use, it is the obligation of the retailer to observe the injunction that the article be dispensed only on prescription.

The fact that the federal law is applicable to the distribution by retailers of drugs which have been in interstate commerce in no way restricts the enforcement of state and local acts relating to the sale of drugs or the practice of pharmacy.

Foreign Letters

LONDON

(From Our Regular Correspondent)

April 17, 1943.

The Proposed National Medical Service

The acceptance by the British Medical Association of the government's invitation to enter into a discussion with the Ministry of Health on a scheme for a comprehensive service for the prevention and cure of disease, available to all members of the community, was reported in a previous letter. In these discussions representatives of other medical bodies than the British Medical Association, such as the medical colleges, are taking part. Though no reports have been published, the declarations of ministers at political meetings enable a forecast to be made. The government proposes that the national health service shall be administered through the local government machinery, which already controls the public health service. This proposal has given rise to the first issue between the profession and the government, for the *British Medical Journal* has in an editorial strongly objected to the proposal, which would place the medical profession under the control of local lay bodies. The alternative is control by some medical body. On the other hand the proposal to create "health centers" for the treatment of disease, where physicians could meet and assist one another and where apparatus would be provided, is welcomed by the profession and was previously recommended by the Medical Planning Commission of the British Medical Association. These centers would be an extension to the whole community of group practice, which already exists as a private enterprise. The free choice of doctor by patients, which already exists under the panel system, has also been announced and is approved in the profession. Thus the time honored British institution "the family doctor" would continue.

In the medical press it is suggested that the mode of payment of the service should be a basic salary for physicians plus a capitation fee. The present sale of practices will come to an end, but compensation for the loss of the investment is demanded. Private practice is not to be forbidden, but as the service is to provide all possible treatment, general and special, hospital and domiciliary, free of charge for every person it seems that private practice must sooner or later disappear. Another question is the position of the voluntary hospitals which were founded and maintained by the money of the charitable for the treatment of the poor. They provide the highest medical and surgical skill, including all kinds of specialism. It is in them that British medicine has been made and in which its leaders, such as Bright, Graves and Hutchinson, to mention only the greatest, made their discoveries. The staffs of these hospitals gave their services free and lived on the consulting practice outside. This must largely or entirely disappear, as consultants are to be supplied under the National Medical Service. They too must look to it for their livelihood. The charitable, who have supported these hospitals in the past, will no longer have any incentive to do so, as the government becomes responsible for all hospital treatment. That is supposing the crushing taxation, which is likely to continue after the war, leaves any money for charity. It seems, therefore, that the voluntary hospitals will be absorbed into the state scheme.

The proposed state medicine for all is indeed a revolution and is much greater than that brought about by the panel system, which applied only to a section of the population. Putting aside a small minority who have socialist views, the scheme is not wanted by the medical profession and is being imposed on it by the government. But opposition to it is voiced by only a few, as it is recognized that the government has the right as well as the power to decide the best system for the promotion of the national health. What physicians can insist on and are insisting on is consultation with them as to details. How the plan arose as part of the Beveridge report on a wide scheme of social reform was shown in a letter in THE JOURNAL, January 9, page 142. It has to be remembered that the plan emanates from a coalition government of all the political parties and is approved by them all. The only political difference is that the labor party has assumed the attitude of being more strenuous than the government and attacked it for want of energy. Thus the medical profession could not rely on the support of any political party if it opposed the scheme.

At a special representative meeting of the British Medical Association the government's invitation to enter into discussions without commitment was agreed to without dissent. A resolution that the section of the population with income above a certain level should continue to obtain domiciliary medical service on a private basis was referred to the council of the association. It was agreed that every practicable step be taken to give all members of the profession, whether members of the association or not, an opportunity to express their views, particularly the members of the profession now on war service.

The Official Medical History of the War

A committee of the war cabinet has been set up to control official histories of the war, of which medical history, including the civilian as well as the fighting services, is to be included. Sir Arthur MacNalty, formerly principal medical officer of the Ministry of Health, is the editor in chief. The director generals of the fighting services will act as editors in respect to their departments. There is a board to supervise the collection of material, prevent overlapping and select contributors. It has power to choose experts on special subjects and consult with investigation committees set up by other bodies, notably the Medical Research Council. Close touch is maintained with various bodies and persons whose work has any bearing on matters of interest for the history. Government departments are cooperating by furnishing reports and official documents relating to medical administration and to technical and clinical subjects. The dominions and colonies and the Allied governments are collaborating. Close liaison has been established with the National Research Council in the United States, which is collecting similar data, and there is an exchange of experience and information. Attention is also being paid to medical literature already published.

Sir Arthur MacNalty has described to the Section of Medicine of the Royal Society of Medicine the scope of treatment of the various medicosociological problems relating to civil life which have arisen during the war. Each of the fighting services will contribute its own section, describing its medical organization before the war, its growth and increased functions during the war, and the medical aspects of the various campaigns. Certain problems will be treated at length in those sections of the history likely to be published first, so that wartime experience may be available as widely as possible. Contributors are being asked to submit progress reports, because few monographs can be written until the war is over. Records should be made while the memory is fresh and changes in methods recorded when they take place. MacNalty indicated some of the headings in the technical volumes: war nutrition, physical training of recruits, effects of shipwreck, immersion and exposure, blood transfusion, effects of high explosive bombs, blast and crush injuries, burns, plastic surgery, epidemiology, venereal diseases, psychiatric conditions, industrial health and rehabilitation. A special volume will be devoted to statistics. He invited the help of the medical profession, on whose cooperation the success of the history would largely depend.

"Deck Ankles"

Under the designation "deck ankles" has been described in the *Journal of the Royal Army Medical Corps* a condition observed on troop ships. On about the tenth day of the voyage some men complain at sick parade of edema of the ankles for which there is no apparent cause. They represent about 1.5 per cent of the total strength on board. It was found that a similar condition had been noted on a previous trip. The swelling appeared insidiously and had no relation to injury. One or both ankles were affected. Some men complained of slight aching and stiffness of the ankles with discomfort and a tired feeling in the feet, especially at the end of the day. In about half the cases the swelling extended on to the dorsum of the foot. It always began at a level just above the edge of the uppers of the gymnasium shoes which had been worn since embarking. In some cases the swelling reached as far as 4 inches above the tips of the malleoli, filling the hollows on each side of the achilles tendon.

No discoloration was noticed at first, but an erythematous flush with fine ecchymoses soon appeared. Active movements were slightly restricted and without pain, passive movements free but slightly painful on full inversion or eversion of the foot. The tissues were mildly inflamed and the skin somewhat hot. No evidence of heart or kidney disease was found, and dietary deficiency was scarcely possible. Rest in bed was thought the most suitable treatment but was impracticable. Some were told to wear boots, and their average number of days on treatment was five; for those who continued to wear gymnasium shoes, twelve days. After the fourteenth day of the voyage the number of cases reporting declined and none reported at the end of the ensuing week. It is suggested that slight trauma, the result of walking on hard decks and repeated small twists of the ankle when ascending and descending hatchways, while wearing gymnasium shoes, produced the disability, that varicose veins, sun erythema and lack of "seasoning" among the troops were aggravating factors and that the wearing of boots, restoring the accustomed support to the ankles, constitutes a specific cure.

The Vector of Indian Kala-Azar Discovered

It has been proved that the sandfly Phlebotomus argentipes is the vector of Indian kala-azar. The discovery is the result of over twenty years' strenuous work in India by a number of investigators. It was early observed that the fly occurs wherever the disease is endemic. It was shown that if the fly is fed on parasite-containing blood of kala-azar patients the disease flagellate forms of Leishmania donovani develop in the foregut and midgut of some of the flies. It was then found that only isolated susceptible animals could be infected by the bites of infected flies, and experiments on human volunteers failed. An impasse seemed to have been reached. How this has been overcome is shown by a paper published in the *Indian Journal of Medical Research* (**30**:473 [July] 1942) by Swaminath, Shortt and Anderson. All five human volunteers were infected by the bites of experimentally infected flies, thus proving that the insect can transmit the disease from man to man. The reason why these experiments were successful appears to be that the flies were sustained during the two weeks development of the parasite in them on fruit juices instead of on blood, as in the previous experiments.

New Type of Air Ambulance for United States Troops in Britain

The United States Eighth Army Air Force has in this country a new type of emergency ambulance aircraft. The machines can be used to accommodate 18 stretcher cases and medical staff or as troop carriers or for carrying freight. The idea is that during the outward journey this big new type should carry troops or equipment, bringing back wounded on the return journey. Air ambulances in Russia and North Africa have saved the lives of many wounded and of sick who would not have survived long and tiring journeys to base hospitals in road ambulances. Aircraft ambulances have also the advantages that they obviate the need for maintaining large stocks of medical supplies in forward positions and that they increase the efficiency of fighting units by relieving them of their responsibility for men put out of action by wounds or illness.

American Surgeon Joins the Editorial Board of the British Journal of Surgery

Col. Elliott C. Cutler, professor of surgery at Harvard Medical School and now chief consultant in surgery to the United States forces in Britain, has accepted a seat on the editorial committee of the *British Journal of Surgery*. In announcing this the *Journal* states that his election is a symbol of the comradeship and brotherhood which unites our countries in the mighty struggle we are waging for the freedom of the world. This step is in accord with the feelings of the late Lord Moynihan, who presided over the policy of the *Journal* for twenty-one years and did incomparable service in bringing together American and British surgeons.

BUENOS AIRES

(From Our Regular Correspondent)

March 3, 1943.

Pulmonary Elasticity

Drs. M. R. Castex, E. S. Mazzei and G. Caputo of the Instituto de Investigaciones Aplicadas a la Palotogía Humana of the Academia Nacional de Medicina of Buenos Aires recently completed certain research work previously carried on with the aim of determining the elasticity of the lung, either normal or in the course of diseases of the respiratory tract. They established the physical conception of elasticity of the structure as the property of the pulmonary tissues to be distended by air and the regaining of their previous form when air is eliminated. The degree of pulmonary elasticity can be determined by (1) the force of distention and (2) the degree of distention which the force provokes. From an analysis of the various methods which have been tried up to now for the determination of the degree of pulmonary elasticity it appears that the Christie and McIntosh method is the most simple, exact and reliable. The standard measures of this method are (1) the intrapleural pressure, which indicates the force of distensibility of the lung, and (2) the volume of current air, which indicates the degree of distention produced. The authors' method is based on two factors. The first factor, the so-called unity of pulmonary distensibility, is the result of the differential figures of the greatest change of pleural pressure between inspiration and expiration, which is measured in centimeters of water. The resulting figure is divided by the volume of current air, which is expressed in hundreds of cubic centimeters. The second factor, which is called the coefficient of pulmonary distensibility, is independent of the size and height of the individual. This factor is the result of the change of intrapleural pressure in a regular respiration. The values obtained by the authors' method are in agreement with those obtained by Christie and McIntosh. The latter established figures between 3 and 4 and 7 and 8 as normal values for the coefficient of pulmonary distensibility and between 0.79 and 1.56 for the unity of pulmonary distention. The authors conclude that the technic of their procedure is simple and the method reliable. It is of value both for the roentgenologist and for the clinician, especially for the diagnosis of borderline cases with signs of fibrosis and accentuated bronchial changes. In anatomic emphysema the figures of the method are always abnormal, whereas the values are normal in cases of functional emphysema, which is frequent in patients with asthma.

Argentine League of Mental Hygiene

The Argentine League of Mental Hygiene was established in 1929. It supports several institutions, especially the Neuropsychiatric Institute, of which Dr. Lefranco Ciampi is the head. The institute has several departments for instruction in the teaching of elementary school as well as of manual and professional work, physical education and orthophonics. The league has two consulting offices for ambulant patients. The number of patients admitted for consultation in the offices increased from 10,000 in 1940 to 13,363 in 1941. The Department of Social Science works in collaboration with the league. The latter has also a school for visiting and social nurses of mental hygiene which has been functioning for the last ten years. It has also an office for juridical consultations. The *Revista Argentina de Higiene Mental*, recently established by the league, will appear quarterly.

Antituberculous Vaccination in Bolivia

A laboratory for the preparation of BCG vaccine was recently established in Sucre, Bolivia, following initiatives of some members of the university of the city. The government of Bolivia recently created a department of antituberculosis vaccination in La Paz. This department depends on the national board for the antituberculosis crusade of the Ministry of Public Health. It is formed by two sections for the preparation and administration of the BCG vaccines respectively. Vaccination should be administered only in certain well organized territories. It will be given under strict conditions of scientific control.

TEL AVIV, PALESTINE

(From Our Regular Correspondent)

Feb. 21, 1943.

Bubonic Plague in Palestine

Since 1922, when bubonic plague appeared as a mild epidemic in Jaffa and in Tel Aviv, Palestine has been free from this disease. In 1922 there were nearly 150 cases, of which about a third proved fatal. The epidemic was quickly brought under control. A dramatic description of the struggle against this epidemic is to be found in Victor Heiser's "An American Doctor's Odyssey." In May 1941 plague infected rats appeared, and in July of the same year the first human case of bubonic plague was reported in Haifa. The report of the Department of Health of the Government of Palestine contains the following interesting details: The trapping and laboratory examination of rats has become a routine procedure in the ports of Palestine since 1920. The value of the measure was shown this year, when, during the first week of May, plague infection was demonstrated in a rodent taken in the port of Haifa. Evidence of increased rat mortality was quickly forthcoming and by the end of the month 11 more infected animals had been collected. Energetic measures were adopted. The harbor is of recent construction and during the building close attention was paid to rat proofing. Conditions were thus favorable for rat destruction, although this was offset at first by the large quantities of grain which were in storage in the sheds. By the end of June no further infected rats were being taken. When an epizootic is established, it is unusual for human beings to escape. and on July 13, in a quarter known as the Eastern Gate, which lies close to the harbor, the first human case occurred. Infected rats were found on the premises, and from then onward spread of infection in both the rodent and the human population was maintained. There were 9 further human cases during the year.

Rat trapping was undertaken over a wide area. In eight months 5,000 rats were trapped, killed or found dead: 66 were infected. Where the harborages of rats permitted of demolition or removal, this was done. Some 4,000 wood and tin shacks were dealt with in this manner. Accumulations of building débris and other rubbish were removed. Rat proofing was undertaken. Houses, shops, cellars, yards, walls and sewers were treated. It is estimated that the equivalent of 800,000 square meters of surface were rendered rat proof. The cost of these operations was £P. 7,000. The operations are being maintained and where necessary extended.

The initial demolitions resulted in the eviction of some 400 families, and this number has since been augmented. Temporary accommodation for a proportion of the families had to be provided. The housing problems do not stop here. Arrangements have been initiated to provide financial assistance for those people, and later perhaps for others living in the slums, who are prepared to replace their shacks by stone built houses. Government credits to the extent of £P. 10,000 have been sanctioned for the purpose.

Existing economic conditions in Haifa present a barrier to the success of the campaign against plague. The soaring rents of recent years have driven people into the slums where conditions, ideal for the rat, are fraught with danger for man.

The methods of rat destruction employed were confined to trapping or killing with batons. Poisoning with bait, smoke and other methods have not yet been adopted. Inoculation with plague vaccine was confined to contacts.

Sulfapyridine therapy was employed early, in doses of 4 Gm. in twenty-four hours for an adult without fatality.

The progress of the disease in each case was swift, and when death occurred it was usually after the first four days. In the fatal cases septicemia set in. In 1 case in which the disease developed exceptionally fast, bacilli were actually found in the sputum. Postmortem examination however, did not reveal pneumonia. It is probable that some cases were not diagnosed in time. Recently, for example, an unidentified Arab, who had been trampled on by a horse, was discovered on a road having died from unknown causes. The autopsy revealed plague bacilli. A diphtheria patient, with characteristic diphtheria membrane in the throat and diphtheria bacilli in the throat, was found to have swollen throat glands. After his death plague bacilli were found in the glands.

One patient was brought to the government hospital with a large open sore on his leg and swollen glands. Under normal circumstances it would not have occurred to the physician to examine the contents of the glands. But his glands were found to contain plague bacilli; plague baccilli were also found in the open sore on his leg.

Large quantities of vaccine are being prepared in the government laboratory and in the university laboratory for the coming spring. Except to a few doctors, plague is an unknown disease to practitioners in this country. In this connection they have been greatly assisted by helpful advice and lectures given by English and Indian military physicians.

Marriages

WILLIAM YASUHI TAKAHASHI, Seattle, to Miss Mary Howard Constable of New York at Ann Arbor, Mich., May 2.

HOWARD VINCENT VALENTINE to Miss Lucille Maureen Decker, both of Spokane, Wash., in Webster, Mass., May 1.

JOHN JOSEPH CREEDON, Flushing, N. Y., to Miss Grace Constance Arbogast of White Plains in New York, May 1.

ALFRED J. NIEDERMAYER, Evansville, Ind., to Miss Violette Capello of Elizabeth, N. J., February 28.

ROBERT LEE ATKINSON, Bloomington, Ill., to Miss Martha Jane Prindle of Evanston in March.

ODEN A. SCHAEFFER, Coral Gables, Fla., to Miss Catherine Louise Smith of Miami, April 11.

ERNEST ROWND, Bogalusa, La., to Miss Reba Pylant of Petersburg, Tenn., April 2.

JOHN G. RUSSO, Madison, Wis., to Miss Pia Camponeschi of Kenosha, March 6.

KENNETH H. SCHNEPP to Miss Lois Catron, both of Springfield, Ill., March 31.

Deaths

Samuel Griffith Davis Jr. ✦ Baltimore; University of Maryland School of Medicine, Baltimore, 1893; specialist certified by the American Board of Anesthesiology, Inc.; member of the American Society of Anesthetists, Inc., and the Association of Military Surgeons of the United States; fellow of the American College of Surgeons; professor of anesthesia at his alma mater; at one time professor of anatomy and operative surgery at the Woman's Medical College of Baltimore; served in the Fifth Regiment of the Maryland National Guard for twenty-six years, as a captain and assistant surgeon in the Spanish-American War and as a major and chief surgeon on the Mexican border; anesthetist to the University, Mercy, Union Memorial, Bon Secours and the South Baltimore General hospitals and the Church Home and Infirmary; consulting anesthetist to St. Joseph's, West Baltimore General and the Sinai hospitals; on the staff of the Hospital for Women; a life-size portrait of "The Three Musketeers" of medicine—Drs. Davis, Guy L. Hunner and Thomas S. Cullen—was presented to the Church Home and Infirmary in 1942 as a gift of the graduate nurses of the institution; aged 75; died, April 21, of heart disease.

Taleasin H. Davies, Wilmington, Del.; University of the South Medical Department, Sewanee, Tenn., 1898; member of the Medical Society of Delaware; a member of the Delaware Commission for Mentally Defective; past president and secretary of the New Castle County Medical Society; for many years a member of the state board of medical examiners; at one time professor of neurology at the Temple University School of Medicine, Philadelphia; formerly superintendent of the Ferris Industrial School; for many years president of the board of health of Wilmington; recently served on the advisory board of the draft board and in the same capacity during World War I; consultant and formerly assistant superintendent of the Delaware State Hospital, Farnhurst; consulting neurologist to the Wilmington General Hospital; chief of the staff of psychiatry and neurology of the Delaware Hospital, where he died, March 25, of lobar pneumonia and cerebral hemorrhage, aged 67.

Hugh Atlee Beam ✦ Moline, Ill.; Northwestern University Medical School, Chicago, 1903; member of the American College of Chest Physicians, and at one time president of the Illinois chapter; fellow of the American College of Physicians; for two years president of the Upper Rock Island County Tuberculosis Association; past president of the Rock Island County Medical Society; served as a captain in the medical corps of the U. S. Army during World War I and as a medical examiner for the draft board for rural Rock Island County; again appointed to the latter position in 1940; member and formerly president of the staffs of the Lutheran and Moline Public hospitals; for many years a medical director of the Rock Island County Tuberculosis Sanatorium, Rock Island; aged 60; died, March 31, in St. Luke's Hospital, St. Louis.

Marion Craig Potter, Rochester, N. Y.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1884; member of the Medical Society of the State of New York; past president of the Women's Medical Society of New York State; one of the members of the committee of medical women of the Council of National Defense during World War I; in 1928 was awarded the Santa Sava medal by the Serbian government for assistance in founding the American Women's Hospital at Monastir; on the staff of the Monroe County Hospital; a delegate to the White House Conference for Child Care and Protection; formerly on the editorial board of the *Medical Woman's Journal*; aged 79; died, March 23, of paralysis agitans.

Walter Elmo Kelton, Seattle; University of Pennsylvania Department of Medicine, Philadelphia, 1905; member of the Washington State Medical Association; served in the medical corps of the U. S. Army during World War I; on the staff of the King County Hospital; in 1935 appointed surgeon to federal prisoners; formerly vice president of the King County Medical Society; surgical consultant, department of labor and industries, for the state of Washington; consultant for the Northern Pacific Railway; aged 65; died, March 9, of coronary thrombosis.

Percy Crump Anders ✦ Plainview, Texas; Birmingham (Ala.) Medical College, 1914; served during World War I; aged 59; died, March 26, of coronary thrombosis.

David F. Banker ✦ Canton, Ohio; Western Reserve University Medical Department, Cleveland, 1900; on the staff of the Mercy Hospital; aged 74; died, March 5, of cardiac decompensation and arteriosclerosis.

Elmer E. Bechtell, Dayton, Ohio; Eclectic Medical Institute, Cincinnati, 1897; member of the Ohio State Medical Association; aged 75; died, March 31.

John Musser Beck, Alexandria, Pa.; Medico-Chirurgical College of Philadelphia, 1901; member of the Medical Society of the State of Pennsylvania; past president and secretary of the Huntingdon County Medical Society; for many years school director of Alexandria and medical inspector of schools of Huntingdon County; a trustee and president of the board of the Memorial Public Library; aged 70; died, March 16, of cardiorenal disease.

James Birckhead, Schenectady, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1899; member of the Medical Society of the State of New York; on the staff of the Ellis Hospital; aged 69; died, March 16, in St. Luke's Hospital, New York, of pneumonia and carcinoma.

William Black ✦ Mankato, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1909; at one time chief of staff of the Immanuel Hospital; aged 64; died, February 12, of hypoplastic anemia.

Max Emanuel Bloch ✦ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; aged 69; died, March 14, in the Illinois Masonic Hospital.

Hughling Ellsworth Bowerman, Leaf River, Ill.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1897; member of the Illinois State Medical Society; served as mayor and as a member of the Ogle County Board of Supervisors; aged 68; died, March 2, in St. Francis Hospital, Freeport, of carcinoma.

Thomas Edward Bowman, Harrisburg, Pa.; Jefferson Medical College of Philadelphia, 1902; member of the Medical Society of the State of Pennsylvania; president of the city Civil Service Board; aged 64; on the staff of the Harrisburg Polyclinic, where he died, March 4, of cerebral thrombosis.

Jacob Bressler ✦ New York; University and Bellevue Hospital Medical College, New York, 1912; on the staff of the Gouverneur Hospital; aged 53; died, March 10, of heart disease.

Charles H. Burgin, Delta, Colo.; American Medical College, St. Louis, 1898; member of the Colorado State Medical Society; city health officer of Delta; formerly member of the board of education; aged 81; died, March 8, of coronary disease.

Dell Duncan Butler ✦ Mount Lebanon, Pa.; University of Pittsburgh School of Medicine, 1918; for many years on the staff of the Western Pennsylvania Hospital, Pittsburgh; aged 48; died, March 3, of coronary thrombosis while shoveling snow.

Vincent P. Capodici, Brooklyn; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1905; aged 62; died, March 3, of cerebral hemorrhage.

James Oliver Carson ✦ Bowling Green, Ky.; University of Louisville Medical Department, 1878; formerly quarantine officer for the Kentucky State Board of Health; served as United States Pension Examiner; member of the board for medical examinations of physicians for the medical corps in the U. S. Army during World War I; fellow of the American College of Surgeons; on the staff of the City Hospital; past president and honorary member of the Rotary Club; aged 87; died, March 15, of heart disease.

Samuel Hopkins Cassidy, Keyport, N. J.; University of Maryland School of Medicine, Baltimore, 1911; president of the board of health of Keyport; aged 63; on the staff of the Royal Pines Hospital, Pinewald, and the Dr. E. C. Hazard Hospital, Long Branch, where he died, March 14, of chronic nephritis and uremia.

Andrew Clark, Billings, Mont.; Detroit College of Medicine, 1893; member of the Medical Association of Montana; aged 78; served on the staffs of the Billings Deaconess Hospital and St. Vincent Hospital, where he died, March 7, of myocardial insufficiency.

Nannie Clayton Clark, San Marino, Calif.; Hahnemann Medical College and Hospital, Chicago, 1889; aged 82; died, March 16, of carcinoma of the stomach.

Jeremiah Joseph Cohane, New Haven, Conn.; Yale University School of Medicine, New Haven, 1898; member of the Connecticut State Medical Society; aged 67; on the staff of the Hospital of St. Raphael, where he died, March 9, of a fracture of the right hip and brain injury received in a fall on the ice.

Brice X. Corbin, Tacoma, Wash.; Washington University School of Medicine, St. Louis, 1898; aged 72; died, March 1, of chronic myocarditis.

Katherine Louise Crawford, Ann Arbor, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1898; aged 84; died, March 16, in Detroit of hypertensive heart disease.

Albert Manning Cross, Charleston, W. Va. (licensed in West Virginia in 1929); served during World War I; formerly on the staffs of the Weston (W. Va.) State Hospital and the Spencer (W. Va.) State Hospital; aged 65; died, February 21, in Hopemont of pulmonary tuberculosis.

Stirley Casper Davis ✠ Tucson, Ariz.; Hospital College of Medicine, Louisville, Ky., 1906; member of the American College of Chest Physicians; fellow of the American College of Physicians; past president of the Pima County Medical Society; one of the founders and chief of the medical staff of the Thomas-Davis Clinic; clinical director of the Southern Pacific Sanatorium; served during World War I; had been president of the school board and of the chamber of commerce; aged 60; died, March 14, of heart disease.

Charles M. Doty, Effingham, Ill.; St. Louis College of Physicians and Surgeons, 1897; member of the Illinois State Medical Society; past president of the Effingham County Medical Society; served as county coroner; aged 72; formerly on the staff of St. Anthony's Hospital, where he died, March 5.

Wilmer Ingalls Gordon, Cleveland; Albany (N. Y.) Medical College, 1887; aged 83; died, March 7, of decompensated heart disease.

Dayton T. Gould, Lodi, Ohio; Western Reserve University Medical Department, Cleveland, 1870; also a pharmacist; chairman of the board of directors of the Berea Commercial and Savings Bank; aged 96; died, March 9, of mitral regurgitation.

Charles Sumner Gracey, Cumberland, Md.; Maryland Medical College, Baltimore, 1912; aged 66; died, March 2, in Everett, Pa.

William Graf, Perrysville, Ohio; Medical College of Ohio, Cincinnati, 1900; aged 74; died, March 2, in the Mansfield (Ohio) General Hospital of thrombosis.

Jesse Trott Grayston ✠ Cedar Rapids, Iowa; University of Illinois College of Medicine, Chicago, 1913; fellow of the American College of Surgeons; served during World War I; on the staffs of the Mercy and St. Luke's hospitals; aged 53; died, March 7, of coronary occlusion.

Francis Freeman Grillet, Alanson, Mich.; Saginaw (Mich.) Valley Medical College, 1900; aged 74; died, March 12, of myocardial insufficiency.

Emil Gunther, Sheboygan, Wis.; Rush Medical College, Chicago, 1892; for a short time served as city physician; aged 75; died, March 8, in St. Nicholas Hospital of cerebral sclerosis, frozen feet and gangrene.

Ernest Hubbard Hamilton, Longview, Texas; University of Nashville (Tenn.) Medical Department, 1900; member of the State Medical Association of Texas; served overseas as a captain in the medical corps of the U. S. Army during World War I; was awarded decorations for bravery; at one time surgeon in the U. S. Public Health Service Reserve; formerly city health officer; chief surgeon for the C. F. Lytle Construction Company, Denison; aged 67; died, March 14, in Denison of bronchopneumonia.

Waldo Russell Harkness ✠ Montpelier, Vt.; University of Vermont College of Medicine, Burlington, 1898; president of the staff of the Heaton Hospital; aged 69; died, March 14, of myocarditis.

Henry Reed Hatfield, Philadelphia; Jefferson Medical College of Philadelphia, 1881; formerly a lawyer; at one time a judge advocate general of the First Brigade, Pennsylvania National Guard, with the rank of major; aged 86; died, March 11, of uremia.

Octavius J. Henderson, Montgomery, W. Va.; Medical College of Virginia, Richmond, 1889; member of the West Virginia State Medical Association; past director of the Montgomery National Bank; aged 79; died, March 13, of pneumonia.

James McPherson Howe, Hillsboro, Iowa; State University of Iowa College of Medicine, Iowa City, 1897; member of the Iowa State Medical Society; aged 73; died, March 11, of myocarditis.

KILLED IN ACTION

MAJ. JOHN JOSEPH MEANY, M. C., U. S. ARMY, 1915-1943

Winfred Harold Iliff, Baxter Springs, Kan.; University of Kansas School of Medicine, Kansas City, 1907; member of the Kansas Medical Society; secretary and past president of the Cherokee County Medical Society; served in the medical corps of the U. S. Army during World War I; aged 59; died, March 2, in St. John's Hospital, Joplin, of pneumonia.

William Henry James, Pennsville, N. J.; University of Vermont College of Medicine, Burlington, 1885; member of the board of health; aged 82; died, March 5, in Philadelphia of arteriosclerosis.

Adolph Samuel Katzman, West Hempstead, N. Y.; University and Bellevue Hospital Medical College, New York, 1902; at one time a druggist; served during World War I; aged 67; died, March 12, of coronary thrombosis.

Claude J. Koonce, Halltown, W. Va.; Georgetown University School of Medicine, Washington, D. C., 1896; aged 72; died, March 12, in the Washington County Hospital, Hagerstown, Md., of lobar pneumonia and agranulocytosis.

Stephen S. Krajewski, Nanticoke, Pa.; Medico-Chirurgical College of Philadelphia, 1911; formerly on the staffs of St. Joseph's and Mercy hospitals, Denver; on the staffs of the Nanticoke State Hospital and St. Stanislaus Orphanage; aged 62; died, March 31, of pneumonia.

Alfred I. Lowenthal, New York; University of Pennsylvania School of Medicine, Philadelphia, 1912; served during World War I; on the staff of the Hospital for Joint Diseases; aged 54; died, March 11, at his home in Leonia, N. J., of cerebral hemorrhage and hypertensive cardiovascular disease.

John Edward Loyd, Natural Bridge Station, Va.; University of Virginia Department of Medicine, Charlottesville, 1901; member of the Medical Society of Virginia; aged 67; on the staff of the Stonewall Jackson Memorial Hospital, Lexington, where he died, March 5, of bronchiectasis.

Louis Emanuel Martin, Savannah, Ga.; Meharry Medical College, Nashville, Tenn., 1909; on the staff of the Charity Hospital; aged 68; died, March 13, of right hemiplegia and nephritis.

Ernest B. McAndrew ✠ Corning, N. Y.; University of Buffalo School of Medicine, 1920; on the staff of the Corning Hospital; aged 47; died, March 15, of coronary thrombosis.

Elam Rowland McBroom, New Canton, Ill.; Chicago College of Medicine and Surgery, 1908; also a methodist minister; veteran of the Spanish-American War; aged 66; died, March 18, of angina pectoris.

John Joseph Meany ✠ Major, M. C., U. S. Army, Bloomington, Ill.; St. Louis University School of Medicine, 1939; served an internship at the St. Louis City Hospital; appointed a first lieutenant in the medical corps of the U. S. Army Feb. 6, 1942; later became a captain, major and flight surgeon with the third air defense wing; aged 27; was killed in action in North Africa, March 20.

Thomas Peacock Miller, Knoxville, Tenn.; Lincoln Memorial University Medical Department, Knoxville, 1910; served as a captain in the medical corps of the U. S. Army during World War I; aged 65; died, March 11, of pneumonia and multiple sclerosis.

Jackson M. Mills, New York; University of Nashville (Tenn.) Medical Department, 1884; Vanderbilt University School of Medicine, Nashville, Tenn., 1884; member of the Medical Society of the State of New York; aged 78; died, March 17, in the New York Hospital of benign hypertrophy of the prostate and bronchopneumonia following transurethral section.

Sydney G. Montell, Jonesboro, Ark. (licensed in Arkansas in 1903); aged 73; died, March 8, of cerebral hemorrhage.

Hassie Albert Moore, Lakeland, Fla.; University of Louisville (Ky.) Medical Department, 1892; aged 83; died, March 19.

William Lawrence Nunan, Philadelphia; Jefferson Medical College of Philadelphia, 1894; on the courtesy staff of the Hahnemann Hospital; aged 73; died, March 23, in St. Luke's and Children's Medical Center of renal calculi, renal infarct and heart disease.

William George Priester ✠ Houston, Texas; Louisville (Ky.) Medical College, 1904; fellow of the American College of Surgeons; on the staff of the Memorial Hospital; aged 61; died, March 20, of acute cardiac dilatation.

Howard Reed, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1891; member of the Medical Society of the State of Pennsylvania; served during World War I; also a pharmacist; at one time on the staffs of the University of Pennsylvania and Temple University hospitals; aged 77; died, March 13, in the U. S. Naval Hospital of carcinoma of the lower part of the intestine.

William Marven Reser, La Fayette, Ind.; Jefferson Medical College of Philadelphia, 1903; member of the Indiana State Medical Association; past president and secretary of the Tippecanoe County Medical Society; a charter member and past president of the Tippecanoe County Historical Society; on the staff of La Fayette Home Hospital; for twenty-five years examining physician for the Prudential Life Insurance Company; aged 79; died, March 19, of pulmonary tuberculosis.

Robert Barnwell Rhett ✠ Charleston, S. C.; Medical College of the State of South Carolina, Charleston, 1914; served in the medical corps of the British Army during World War I; major in the medical reserve corps of the U. S. Army not on active duty; associate in ophthalmology, rhinology and otolaryngology at his alma mater; on the staff of the Roper Hospital; aged 52; died, March 23, of myocarditis and angina pectoris at his summer home near Hendersonville, N. C.

John Frederick Rickenbach, Pittsburgh; Bellevue Hospital Medical College, New York, 1875; aged 94; died, March 19, in the German Protestant Home for Aged of heart disease.

Edgar Rood, Westfield, N. Y.; University of Buffalo School of Medicine, 1878; aged 89; died, March 7, in Buffalo of angina pectoris.

Hugh Madison Ross, Chester, S. C.; Medical College of the State of South Carolina, Charleston, 1911; served during World War I; aged 56; died, March 14, in the Pryor Hospital of ruptured diverticulitis.

Belle Bennett Sharpe, Pasadena, Calif.; Hahnemann Medical College and Hospital, Chicago, 1905; aged 74; died, March 14, of cerebral hemorrhage and arteriosclerosis.

Charles Wade Simison, Hawley, Minn.; University of Missouri School of Medicine, Columbia, 1907; member of the Minnesota State Medical Association; in 1938 elected vice president of the Northern Minnesota Medical Association; member of the sanitarium commission in Clay and Becker counties; aged 64; on the staff of St. Ansgars Hospital, Moorhead, where he died, March 6, of cerebral hemorrhage.

Clarence Elmer Smith ✠ Massillon, Ohio; Ohio Medical University, Columbus, 1902; member of the city board of health; aged 67; on the staff of the Massillon City Hospital, where he died, March 9, of cerebral hemorrhage.

Edward Cooper Smith, Donalsonville, Ga.; Atlanta College of Physicians and Surgeons, 1907; member of the Medical Association of Georgia; served as mayor of Donalsonville and as president of the chamber of commerce; aged 58; died, March 15, in Dothan of carcinoma of the lung.

Charles Wadhams Stevens ✠ New York; College of Physicians and Surgeons, New York, 1892; formerly assistant professor of clinical ophthalmology at the New York Post-Graduate Medical School, Columbia University; veteran of the Spanish-American War; captain in the medical reserve corps of the U. S. Army not on active duty; for many years on the staff of the New York Post-Graduate Medical School and Hospital; aged 75; died, March 15, of heart disease.

George Edward Stevenson, Penn Yan, N. Y.; Baltimore Medical College, 1895; member of the Medical Society of the State of New York; served during World War I; on the staff of the Soldiers and Sailors Memorial Hospital; aged 72; died, March 20, of coronary occlusion.

Le Roy Ray Stoddard, New York; New York Homeopathic Medical College and Hospital, New York, 1900; aged 66; was found dead in a hotel in Baltimore, March 18, of chronic myocardial degeneration.

Benjamin Strong, Lamar, Miss.; University of Pennsylvania Department of Medicine, Philadelphia, 1891; member of the Mississippi State Medical Association; aged 79; died, March 15, of carcinoma of the stomach.

Hugh Nathan Sullivan, Ellendale, Tenn.; Memphis Hospital Medical College, 1906; aged 60; died, March 14, in Memphis of arteriosclerosis and heart disease.

Albert Hamlet Sweeney, Fresno, Calif.; Cooper Medical College, San Francisco, 1897; formerly health officer of Fresno; for twenty-five years division surgeon for the Santa Fe Railroad; aged 73; died, March 1, of heart disease.

Sherman Clark Sweeting, Pavilion, N. Y.; Hahnemann Medical College and Hospital, Chicago, 1890; health officer of the towns of Covington, Bethany and Pavilion; aged 77; died, March 18, in the Wyoming County Community Hospital, Warsaw, of heart disease.

Joshua Tayloe ✠ Washington, N. C.; University of Pennsylvania School of Medicine, Philadelphia, 1923; fellow of the American College of Surgeons; past president of the Beaufort County Medical Society and the North Carolina Urological Society; vice president of the Seaboard Medical Society; chief of staff of the Tayloe Hospital; aged 44; died, March 5, of coronary thrombosis.

Arvid Ouchterlony Taylor ✠ Maysville, Ky.; University of Louisville Medical Department, 1906; formerly member and president of the board of education of Maysville; a member of the Mason County Board of Health; aged 59; died, March 9, of coronary occlusion.

Charles Byron Ward ✠ Seattle; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1908; specialist certified by the American Board of Radiology, Inc.; member of the American Roentgen Ray Society, the Radiological Society of North America, Inc., and the American College of Radiology; aged 60; on the staff of the Providence Hospital, where he died, March 28, of coronary thrombosis.

Benjamin N. Watt, Washburn, Ill.; Rush Medical College, Chicago, 1884; aged 88; died, March 10, of cerebral hemorrhage.

Villiers James Webber ✠ Fairhope, Ala.; American College of Medicine and Surgery, Chicago, 1906; served during World War I; aged 64; died, March 8, of pellagra.

Nels Werner ✠ Eau Claire, Wis.; Rush Medical College, Chicago, 1904; for many years on the staff of the Midelfart Clinic; on the staffs of the Luther and Sacred Heart hospitals; aged 63; died, February 26, of heart disease.

Jesse David Westmoreland, Belzoni, Miss.; Memphis (Tenn.) Hospital Medical College, 1904; aged 68; died, March 17, in the King's Daughters' Hospital, Greenville, of cerebral hemorrhage.

Florilla Mansfield White, Palm Springs, Calif.; Boston University School of Medicine, 1908; aged 71; died, March 15, of cerebral hemorrhage and arteriosclerosis.

DIED WHILE IN MILITARY SERVICE

Robert Anthony Kilduffe ✠ White Sulphur Springs, W. Va.; University of Pennsylvania School of Medicine, Philadelphia, 1913; member of the American Society of Clinical Pathologists, the Society of American Bacteriologists and the Association of Military Surgeons of the United States; formerly vice president of the New Jersey Society of Clinical Pathologists; served in France as chief of the bacteriologic division on the staff of the chief surgeon of the American Expeditionary Forces during World War I; formerly director of the laboratories of the Pittsburgh Hospital; while a resident of Atlantic City, N. J., was director of the laboratories of the Atlantic City Hospital and city bacteriologist, serologist to the Municipal Hospital and the Atlantic County Hospital for Mental Diseases, Northfield, pathologist and serologist to the Betty Bacharah Home for Crippled Children and pathologist to the Jewish Seaside Home for Children; began active duty Oct. 1, 1942 as a major in the medical corps of the Army of the United States, assigned to the Ashford General Hospital as chief of the laboratory service; editor of the *American Journal of Clinical Pathology*; associate editor of the *Journal of Laboratory and Clinical Medicine* and of the *International Medical Digest;* author of several manuals of laboratory procedure; co-author of "The Blood Bank and Technique and Therapeutics of Transfusion"; aged 58; died suddenly, April 5, of coronary occlusion.

CORRECTION

Dr. Edward Herzog Is Not Dead.—Information has been received that Dr. Edward Herzog of Long Island City, N. Y., is living. THE JOURNAL, March 6, page 781, erroneously reported the death of Dr. Herzog.

Correspondence

ARMY-NAVY MEDICAL TRAINING PROGRAM

To the Editor:—The "sweeping new" Army-Navy program, proposed to go into effect this June, deserves some comment at this time. The program includes fifteen months of "premedical" education and three years of concentrated formal medical education followed by a year of internship.

The practice of medicine is still both an art and a science. The country doctor, of whom the whole profession is proud, practiced more of the art than the science. But, to practice the art of medicine requires two essentials: culture and maturity. Today is an age of dehydration and compression, but neither culture nor maturity can be compressed. As far as the science is concerned there are many men, not of the production line species, who are still learning after years of faithful application. The scientific method demands background, experience and attention to detail.

I am not so far removed from my school days to remember that I spent a considerably longer period than fifteen months to master the elemental sciences. I recall that I spent a considerably longer time to acquire what little culture I have. It might also be noted that I emerged from school capable of thought and insight into the physician's responsibilities to society.

Dr. O. H. Perry Pepper, anticipating that our nation was approaching a crisis, sounded the note that we attempt to continue our education by our own efforts. He had the foresight to see that war would prevent one from entering the specialties as he delivered his final lecture to the graduating class. The plea of a great teacher to well educated men probably was made because he must have known that their experience was only beginning, not after five and one-quarter years of "compressed" education, but after nine years of learning.

There are young men in our colleges now who want to study medicine. There are also men who would study medicine to escape more arduous tasks rather than out of a humanitarian bent. Let us beware that among the good barrel of apples rotten ones do not occur. This, then, is the plea that the standards and quality of our learning be maintained. Let us not forget we are mature in thought and that a heritage of culture has been passed on to us, not by education but by learning.

THOMAS MAXWELL, First Lieutenant, M. C., A. U. S.

"Q FEVER"

To the Editor:—My attention has been called to an article in THE JOURNAL (March 13, p. 828) entitled "Q Fever." Since the basis for the diagnosis of Q fever in this reported case was certain serologic tests done in this laboratory, I feel that two comments should be made: First, the diagnosis of Q fever was made on a complement fixation test the titer of which was only 1:4. Those interested in this test at this laboratory feel that such a titer is not significant, particularly during the acute illness or early in the convalescence. Second, the article reports other serologic tests done at this laboratory but fails to mention that an agglutination of 1:80 against Eberthella typhosa was obtained. This was on a sample of serum submitted on August 11, some two and one-half weeks after onset (July 25). In the case report there was no record of additional studies done later in the forty-six day febrile illness.

It is felt then that this case, reported as Q fever, certainly had no confirmation in the laboratory and further that it was more suggestive of belonging to the group of long continued fevers than to the rickettsioses.

R. E. DYER, M.D., Bethesda, Md.
Director, National Institute of Health.

[On receiving a copy of Dr. Dyer's communication, the author replied:]

To the Editor:—I appreciate your sending me the criticism of my paper on Q fever. With regard to the omission of the typhoid test being positive 1:80, it is truly an omission that I was entirely unaware of. Fortunately I had saved all my data and many copies of the paper as it was written. The paper was rewritten and corrected many times in order to get it in correct form and that test was in the first typewritten copy, but evidently my secretary in recopying it several more times omitted it accidentally along with B paratyphoid A negative. In fact the entire line was omitted and I did not realize it until now. I was careful to be as exact as possible and to give credit where credit was due. You will note that the stool culture for typhoid also was negative.

As to the positive complement fixation test for Q fever 1:4, I asked about this in both of our hospital laboratories at the time, and it was felt that a 1:4 complement fixation test was definitely positive. I was not familiar with this test, as it was new and I know little about the details of such a test but am surprised that it was not considered a positive test.

The criticism is rather severe and not entirely correct, as a clinical diagnosis was temporarily made on the finding as described in Manson's Tropical Diseases on Q fever. The following correction should be made because of the omission: Blood serum taken on Aug. 11, 1942 was reported as follows on August 22. Eberthella typhosa positive in dilution 1:80 and Eberthella paratyphosa A negative. To my mind this does not alter the case, for the weight of evidence points to Q fever.

The omission was accidental and if the complement fixation test of 1:4 was not conclusive, it was ignorance on my part.

F. EUGENE ZEMP, M.D., Columbia, S. C.

IRRADIATION OF THE SPLEEN AND PITUITARY FOR CONTROL OF PUBERAL BLEEDING

To the Editor:—Some inaccuracies in the article by Dr. Ira I. Kaplan in THE JOURNAL of April 10 require comment and adjustment. Irradiation of the pituitary gland for the control of uterine bleeding in the adult was first advocated by me in 1922 and 1923 (*Arch. f. Gynäk.* **117**:230, **120**:194). This entirely new method was based on clinical and experimental evidence showing impairment of the development and the integrity of structure and function of the female generative tract as the result of destruction of the anterior lobe of the hypophysis or of damage to the midbrain. The fact that no harm may result from the application of properly screened hard roentgen rays to the brain of the adult emerged from the careful studies of Heineke, Lacassagne and Birch-Hirschfeld, while the investigations of Obersteiner revealed that the less resistant brain tissue of the adolescent organism may sustain microscopically demonstrable damage. Initially, suppression of abnormal pituitary stimuli to the ovaries and hence regulation of excessive uterine bleeding constituted my professed purpose in applying x-rays to the hypophysial region. The results obtained with this novel treatment eloquently demonstrated the usefulness of the procedure. In view of my experimental evidence showing a distinct relationship between excessive anterior pituitary hormone activity and small cystic ovarian degeneration resulting in the overproduction of estrogenic substances and in turn of endometrial overgrowth (*Surg., Gynec. & Obst.* **22**:222 [Feb.] 1931; *J. Obst. & Gynec. Brit. Emp.* **46**:232 [April] 1939), a check on the pituitary impulse by irradiation appeared an obvious rationale. Indeed, satisfactory relief of polycystic ovaries by the treatment under consideration has been reported (Stein, I. F., and Leventhal, M. L.: *Am. J. Obst.* **29**:181 [Feb.] 1935).

Further elaboration revealed numerous startling phenomena. As stated in the two articles which I have referred to, some uterine fibroids which had been irradiated directly before shrank considerably after one or two irradiations of the hypophysis. The reports which I published were substantiated by other observers, indicating that the growth hormone of the anterior pituitary may bear some etiologic relationship to the origin of such tumor formation. Increase of the red blood count and the number of eosinophils represented another remarkable phenomenon. Particular interest attached to the observations which I made of reduction in the size of the hyperplastic thyroid following pituitary irradiation. In the light of the demonstration of the thyrotropic principle residing in the anterior pituitary some years afterward, the explanation of this phenomenon as due to the suppression of the hyperactivity of this principle offered itself. Treatment of hyperthyroidism by pituitary irradiation was advocated twelve years later by Borak (*Radiology* **24**:535 [May] 1935). It is worthy of note that quite recently this novel thought of influencing the hyperplastic thyroid by hormones directly or indirectly related to the hypophysis has come to the fore (Alton Ochsner). Incidentally, it is pertinent to note the influence which pituitary irradiation has exercised on other conditions, such as on the radiosensitive basophilic infiltration in posterior lobe hyperfunction (Pendergrass, Hodes and Griffith: *Am. J. Roentgenol.* **46**:673 [Nov.] 1941; Hutton; Cushing). On the other hand, clinical observations of the occurrence of diabetes insipidus, if temporary, and of adiposogenital atrophy (H. Hirsch) in the wake of pituitary irradiation in young persons provided a warning note that this treatment should be used with discernment. In harmony with the experimentally established fact mentioned that the brain of the growing organism may be injured by the application of radiant energy, I feel that pituitary irradiation has no place in the treatment of gynecologic disorders in persons under 20 years of age irrespective of "the dosage and method properly selected."

J. I. Hofbauer, M.D., Cincinnati.

COLOR BLINDNESS IN PHYSICIANS

To the Editor:—In THE JOURNAL, April 17, I noted a query in regard to a medical student who is color blind. I claim to be an authority on the vicissitudes of color blind doctors and would like to give him the benefit of my experience. In 1917 I was rejected for the Army because of color blindness. In 1918 I was accepted as a flying cadet and served out the duration without being bothered with any colors at all. In 1926 misfortune caught me again when I attempted to obtain a commission in the Medical Corps and I was rejected for color blindness. This discouraged me somewhat, and I have not been encouraged any by remarks of present day Army and Navy medical examiners. I have never had any difficulty in the practice of medicine other than in laboratory work, and I didn't like that anyway. Now, as to laboratory work, I accept tubercle bacilli and mitotic figures on faith alone, never having been able to see any. I would suggest to the student who is color blind that he be nice to the student next to him in the laboratory, preferably a female, and she will prove of inestimable value to him when it comes to colorimeters and such like. Also don't try to join the Navy or Air Force, as they are God's elect and won't have any color blind misfits. One other point: When he gets out of school, all of his friends will on occasion grab some piece of colored cloth and demand to know what color it is. This, I think, is justifiable ground for homicide. In conclusion, never argue with the Ishihara color test because he will always be wrong. However, we can see a lot of things in that which normal individuals can't see, so why worry?

G. A. DAVIDSON, M.D., Dallas, Texas.

MEDICAL VOLUNTEERS FROM BROOKLYN

To the Editor:—I noted with chagrin the inclusion of Brooklyn in the list of cities mentioned by you editorially on March 27 as one in which the number of physicians responding to the call of the Procurement and Assignment Service was far below quota. I feel quite sure that your inclusion of Brooklyn in this list was because of the fact that you were not in possession of the exact factual data, which I therefore herewith enclose. The total number of doctors in Brooklyn is 5,190, of which total there are now 2,004 in active service with the Army or Navy and about 50 more in other government services. There are about 81 more in process of receiving their commissions. You will note, therefore, that this would make 41 per cent of physicians in Brooklyn under the age of 64 in active government service. You will agree, I am sure, that this is an enviable record of which we are duly proud.

BENJAMIN M. BERNSTEIN, M.D., Brooklyn.
Secretary, Medical Society of the County of Kings.

COMMENT.—On Nov. 30, 1942, metropolitan New York, which included Bronx, Kings, Nassau, New York, Queens, Richmond, Rockland, and Westchester counties, still required 3,307 physicians to fill their quotas. Since that time there have been less than 1,000 physicians who have gone to active duty from the entire state of New York. Apparently most of the shortages are in other counties than Kings.—ED.

SIMPLIFIED TECHNIC IN CONTINUOUS CAUDAL ANALGESIA

To the Editor:—Caudal analgesia in obstetrics as advocated by Drs. Hingson and Edwards is the second great step for the amelioration and the alleviation of the pain and anguish of childbirth. The first was the introduction of chloroform to the practice of obstetrics.

My limited experience with caudal block has been satisfactory thus far to the women and to me.

There will, of course, be many improvements in the original technic. The principal purpose of the apparatus used and described by the originators was to maintain a closed aseptic circuit and for the maintenance of a constant analgesic affect during all of the labor after the first insertion of the needle into the caudal canal.

I should like to describe a simpler closed circuit technic that can be used and watched over by personnel trained in obstetrics other than the attending obstetrician or anesthetist, the purpose being to make caudal analgesia available to all, the private, semiprivate and ward patients. Most hospitals have personnel well versed in determining the progress of labor; this trained group can well be entrusted with the added duty of watching over the effects of caudal analgesia.

The original technic as described by Hingson and Edwards is followed through the injection of 8 cc. of metycaine. At this point the technic varies. The syringe is disengaged from the caudal needle. A sterilized 2 inch rubber tube, closed at one end with an adapter to fit the needle at the other end, is fitted by its adapter into the needle hub and a closed sterile circuit is instantly created. The next 22 cc. of metycaine and all subsequent instillations are made through injections directly into the rubber tubing, which has first been wiped clean and sterilized with alcohol in much the same manner as any subcutaneous or intravenous injection.

After the insertion of the needle into the rubber tubing, slight negative pressure created by traction on the syringe piston can show whether there is any spinal fluid leakage. Following each instillation of metycaine the protruding needle hub with the attached rubber tube is wrapped in soft cotton and held in the fold of the buttocks with a few strips of adhesive tape.

J. A. MILLER, M.D., New York.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, May 22, page 252.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 15-16. Sec., Dr. B. F. Austin, 519 Dexter Ave., Montgomery.

ARIZONA: * Phoenix, July 6-7. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: * *Medical.* Little Rock, June 3-4. Sec., Dr. D. L. Owens, Harrison. *Eclectic.* Little Rock, June 3-4. Sec., Dr. C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Written.* San Francisco, June 28-July 1. *Oral.* Los Angeles, August 9. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento.

COLORADO: * Denver, July 7-9. Final date for filing application is June 20. Sec., Dr. J. B. Davis, 831 Republic Bldg., Denver.

CONNECTICUT: * *Written.* Hartford, July 13-14. *Reciprocity.* Hartford, July 27. Sec. to the Board, Dr. Creighton Barker, 258 Church St., New Haven. *Homeopathic.* Derby, June 8-9. Sec., Dr. J. H. Evans, 1488 Chapel St., New Haven.

DELAWARE: Dover, July 13-15. *Reciprocity.* Dover, July 20. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

FLORIDA: * Jacksonville, June 21-22. Sec., Dr. William M. Rowlett, Box 786, Tampa.

HAWAII: Honolulu, July 12-15. Sec., Dr. J. A. Morgan, 55 Young Building, Honolulu.

IDAHO: Boise, July 13. Dir., Bureau of Occupational Licenses, Mrs. Lela D. Painter, 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, June 22-24. Superintendent of Registration, Department of Registration and Education, Mr. Philip M. Harman, Springfield.

INDIANA, Indianapolis, Sept. 14-16. Sec., Board of Medical Registration & Examination, Dr. W. C. Moore, 301 State House, Indianapolis.

KENTUCKY: Louisville, Nov. 15-17. Sec., Dr. A. T. McCormack, 620 S. Third St., Louisville.

MAINE: Augusta, July 6-7. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Homeopathic.* Baltimore, June 15-16. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, July 13-16. Sec., Board of Registration in Medicine, Dr. H. Q. Gallupe, 413-F State House, Boston.

MICHIGAN: * Ann Arbor and Detroit, June 9-11. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 100 W. Allegan St., Lansing.

MONTANA: Helena, Oct. 5-6. Sec., Dr. O. G. Klein, First Nat'l Bank Bldg., Helena.

NEW HAMPSHIRE: Concord, Sept. 9-10. Sec., Board of Registration in Medicine, Dr. D. G. Smith, State House, Concord.

NEW JERSEY: Trenton, June 15-16. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: * *Endorsement.* Santa Fe, Oct. 11-12. Sec., Dr. LeGrand Ward, 141 Palace Ave., Santa Fe.

NORTH CAROLINA: Raleigh, June 14-18. Sec., Dr. W. D. James, Hamlet.

NORTH DAKOTA: Grand Forks, July 6-9. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: *Endorsement.* Columbus, July 7. *Written.* Columbus, Dec. 4. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

RHODE ISLAND: * Providence, July 1-2. Chief, Division of Examiners, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, June 28-30. Sec., Dr. N. B. Heyward, 1329 Blandena St., Columbia.

SOUTH DAKOTA: * Pierre, July 20. Act. Dir., Medical Licensure, State Board of Health, Dr. A. Triolo, Pierre.

TEXAS: Dallas, June 1-3. Sec., Dr. T. J. Crowe, 918-20 Texas Bank Bldg., Dallas.

UTAH: Salt Lake City, June 2-4. Dir., Department of Registration, Mr. G. V. Billings, 324 State Capitol Bldg., Salt Lake City.

WEST VIRGINIA: Charleston, July 6-8. Commissioner, Public Health Council, Dr. C. F. McClintic, State Capitol, Charleston.

WISCONSIN: * Milwaukee, June 29-July 1. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.

WYOMING: Cheyenne, June 7-8. Sec., Dr. M. C. Keith, Capitol Building, Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: Tucson, June 15. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson.

COLORADO: Denver, June 9-10. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver.

CONNECTICUT: June 12. Address State Board of Healing Arts, 250 Church St., New Haven.

DISTRICT OF COLUMBIA: Washington, Oct. 18-19. Sec., Dr. G. C. Ruhland, 6150 E. Municipal Bldg., Washington.

FLORIDA: DeLand, June 9. Final date for filing application is May 24. Sec., Dr. J. F. Conn, John B. Stetson University, DeLand.

IOWA: Des Moines, July 13. Dir., Division of Licensure & Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MICHIGAN: Ann Arbor and Detroit, June 4-5. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing.

NEW MEXICO: June 14. Sec., Miss Pia Joerger, State Capitol, Santa Fe.

OREGON: Corvallis, July 10. Sec., State Board of Higher Education, Mr. C. D. Byrne, University of Oregon, Eugene.

SOUTH DAKOTA: Aberdeen, June 4-5. Sec., Dr. G. M. Evans, Yankton.

WISCONSIN: Milwaukee, June 5. Sec., Prof. R. N. Bauer, 152 W. Wisconsin Ave., Milwaukee.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Hospitals in General: A Hospital Not a "Public Housekeeping Establishment" Within Meaning of State Minimum Wage Law.—The plaintiff was employed in March 1937 by the Trinity Hospital Association of Minot, N. D., a nonprofit corporation, as a "public housekeeper" at a monthly stipend, after the first five weeks, of $20 plus board, room (which she apparently never utilized), laundry and free hospitalization in case of sickness. The North Dakota minimum wage and hour law, as amended (Laws 1935, ch. 162) empowers the commissioner of agriculture and labor to ascertain and declare minimum wages, and the commissioner, acting in pursuant thereof, promulgated a so-called Order No. 1, which provided stated minimum weekly wages for various types of employees in "public housekeeping establishments" in the state, the applicable minimum of which exceeded the equivalent periodical stipend of the plaintiff. She subsequently brought suit against the hospital to recover the difference between the wages paid her during the period from 1937 to 1940 and the applicable minimum set out in Order No. 1. The hospital denied liability, defending principally on the ground that the order relied on by the plaintiff did not apply to employment in nonprofit hospitals in North Dakota. From a judgment for the plaintiff the hospital appealed to the Supreme Court of North Dakota.

The sole question for our determination, said the Supreme Court of North Dakota, is whether or not the plaintiff is within the class of employees covered by Order No. 1. Order No. 1 refers only to employees of any "public housekeeping establishment." No other class of employees is included. Therefore, the plaintiff to claim the benefit of Order No. 1 must bring herself within the class of employees covered by the order. The word "hospital" in general usage in the minds of the public is an institution in which the sick and injured are cared for. It is a place where patients receive medical attention. It is not a place like an inn or hotel where people go for food and entertainment. It is true, a hospital must serve food to its patients, as an incident to their care and treatment, but it is not a public housekeeping establishment. Only the sick or injured are admitted to a hospital; it is not open to the public generally like a restaurant or hotel. The difference between a public housekeeping establishment, such as a hotel, inn or restaurant, and a hospital is clearly explained by the Supreme Court of Iowa in *Hull Hospital* v. *Wheeler*, 216 Iowa 1394, 250 N. W. 637. In that case a patient in the Hull Hospital in addition to care, medicine and hospital supplies received board and room. The hospital sought to obtain an innkeeper's lien on certain rings belonging to the patient left in the custody of the hospital. By Code, Iowa, 1930, Section 10348, a hotel is given a lien on the baggage of its guests and "hotel" is defined to "include inn, rooming house, and eating house, or any structure where rooms or board are furnished, whether to permanent or transient occupants." The Supreme Court of Iowa there said:

> Although the definition of the word "hotel" is thus extended, nevertheless there is a plain limitation upon the kind of business that shall constitute a hotel. A hotel keeper entertains his guests. He furnishes them food, drink, shelter, and lodging. Likewise, an eating house furnishes its patrons food and drink. So, too, a rooming house provides the roomer with lodging and shelter. . . .
>
> On the other hand, a hospital, where the sick and injured are cared for, nurses its patients and gives them medical attention. . . . Obviously the room and board provided by the hospital are merely incidental to the nursing and medical treatment, if not part of it. For instance, a guest goes to a hotel for lodging, shelter, food, and drink. Such is the purpose of the hotel. When a man is sick, however, he goes to the hospital, not merely for food, drink, lodging, and shelter, but rather for nursing and medical care. . . .
>
> Plainly, therefore, the appellant [the hospital] is not entitled to a lien on the rings in the case at bar because a hospital is not a hotel.

While hotels, restaurants and inns, continued the Supreme Court of North Dakota, may come under the classification of "public housekeeping establishments," since the main purpose of such institutions is to furnish food, shelter and entertainment to guests, a hospital is not a "public housekeeping establishment,"

since its main purpose is to care for and give medical attention to sick, wounded and injured patients. The legislature in the passage of the minimum wage and hour law did not make it mandatory on the commissioner of agriculture and labor to take jurisdiction of all employees in the state. So far the commissioner has not made any order covering employees of a hospital, and therefore there is no basis for recovery here. Whether or not the commissioner has a legal right to promulgate orders covering employees of charitable nonprofit corporations, therefore, is not involved in this case.

The judgment in favor of the hospital employee was reversed. —*Pagel v. Trinity Hospital Ass'n, 6 N. W. (2d) 392 (N. D., 1942).*

Workmen's Compensation Acts: Inhalation of Sewer Gas as Efficient Cause of Perforation of Duodenal Ulcer. —Dauber was able to work, although suffering from a stomach ulcer causing a pyloric obstruction, on a diet prescribed for him by Dr. Bank, a "stomach specialist," whom he consulted in June 1941. In the course of his employment with the City of Phoenix, Ariz., on Oct. 4, 1941, he was cleaning out a sanitary sewer pipe line. It was his duty to descend into a manhole to clean out the mud and slush that would be forced down the pipe line by water pressure and rodding against a funnel-shaped object made of canvas. Sewer gas was released by this process and passed through the opening in the top of the pipe into the manhole. While in a manhole about 3 p. m. "all of a sudden a cloud of gas come in" and rendered the workman unconscious. He was pulled out of the manhole. When he regained consciousness about fifteen minutes later he was greatly nauseated and began vomiting. He was taken home and put to bed but continued to suffer from severe nausea. Dr. Shupe was called in about 8 o'clock that evening and administered morphine "to quiet him and decrease his vomiting." However, the nausea returned as soon as the effect of the narcotic wore off, and about 10 p. m. the following evening he was taken to a hospital. Nausea nevertheless continued until about 8 p. m. on October 6, "when a perforation of his stomach occurred followed by severe peritonitis." Immediately afterward Shupe performed an emergency operation and repaired the perforation. Dauber was still totally disabled at the time of a hearing held on Feb. 11, 1942, in proceedings he instituted to recover compensation under the workmen's compensation act of Arizona. At the hearing Dr. Bank, whom Dauber had consulted the previous June, testified that in his opinion inhaling the sewer gas would aggravate the ulcer from which Dauber was suffering and that a perforation of an ulcer of the stomach is caused by aggravation of the ulcer. Dr. Shupe testified that sewer gas poisoning induces nausea and vomiting and that in his opinion inhaling the sewer gas was the efficient cause of the rupture of the ulcer from which Dauber was suffering at the time of the alleged accident. The industrial commission, however, denied compensation on the ground that the evidence did not show that the disability from which Dauber was then suffering was the result of an accidental injury sustained while in the course of his employment. It reaffirmed its denial of compensation on a rehearing held about three months later, and Dauber appealed to the Supreme Court of Arizona.

Dauber contended that his mishap was an accident within the meaning of the workmen's compensation act and that the action of the commission was contrary to the evidence and should be set aside. It is elementary, of course, said the court, that Dauber before he is entitled to compensation must show that his injury was the result of an accident within the meaning of the workmen's compensation act. The court was of the opinion that the sudden and unexpected coming into the manhole of a cloud of sewer gas in sufficient quantity to render Dauber unconscious was an accident within the meaning of that term as used in the workmen's compensation act. Even though a small quantity of gas, said the court, is usually looked for in such places as those in which Dauber was working, the sudden appearance of such a quantity of it as to render him unconscious was wholly unexpected. Neither Dauber nor any one else who thought the gas might escape into the manhole in such dangerous quantities during the process of cleaning the sewer pipe would have ventured into the manhole where he would breath it with such serious consequences. Dauber had smelled the gas many times before in small quantities, but this was the first time that a cloud of it had come into the manhole where he was working and, this being true, it cannot be said that he should have known it would be there in such a dangerous quantity and that he assumed whatever risk there was in contacting it. As was said in *Van Vleet* v. *Public Service Company of York,* 111 Neb. 51, 195 N. W. 467:

> While the evidence shows that gassing in a mild form is not uncommon among gas workers, it is equally proved that for workmen to be overcome to such an extent as to produce unconsciousness is very uncommon.

A somewhat similar statement is also found in Taylor's Principles and Practices of Medical Jurisprudence, volume 2, page 573, where, in a discussion of poisoning by sewer gas and exhalations from dead bodies, the following statement is made:

> The cases are always accidental, though it is easily conceivable that a suicide or homicide might thus be effected.

Hence, the passing into the manhole of a cloud of gas which rendered Dauber unconscious was an untoward and unexpected event and clearly constituted an accident within the meaning of the compensation act.

The next question, said the court, is whether or not the accident resulted in injury to Dauber. The testimony of the only two physicians who appeared as witnesses in the case is that the inhalation of the sewer gas had the effect of perforating and rupturing his stomach and that this necessitated an emergency operation. The two physicians agreed that the nausea, retching and vomiting produced by the accident caused the injury. According to Dr. Shupe the retching and vomiting were the efficient cause of the rupture of the stomach ulcer, though Dr. Bank's view was that, while the retching and vomiting were factors in producing the rupture, the more important factor was the absence of food, which, because of acid, increased erosion of the stomach. So whether the rupture was produced by the retching and vomiting or by the absence of food in the stomach for so many hours is immaterial, since both of these conditions were the result of the nausea and vomiting brought about by the accident, the inhalation of the sewer gas. The fact that the gas itself may not have been the direct cause of the rupture is immaterial; it would be just as much the efficient cause thereof if it set in motion the agencies that did produce it—nausea, retching and vomiting—as it would have been had it caused it directly, and there can be no question but that the nausea, retching and vomiting were brought about by the accident. The fact that at the time of the accident, and for some months prior thereto, Dauber had been suffering from a duodenal ulcer did not deprive him of the right to compensation, since the accident was the cause of the rupture, for even though the perforation of the stomach would not have resulted from the accident had it not been for its weakened condition produced by the ulcer, his right to compensation for the injury was in no way affected thereby. When an accident aggravates a diseased condition, the rule established by the decisions of this court is that the workman is as much entitled to compensation for the injury as he would have been had it occurred while he was in a healthy condition.

The court accordingly set aside the award of the industrial commission denying compensation to the workman.—*Dauber v. City of Phoenix, 130 P. (2d) 56 (Ariz., 1942).*

Society Proceedings

COMING MEETINGS

HOUSE OF DELEGATES OF THE AMERICAN MEDICAL ASSOCIATION, CHICAGO, BEGINNING JUNE 7. DR. OLIN WEST, 535 NORTH DEARBORN ST., CHICAGO, SECRETARY.

American Association of Genito-Urinary Surgeons, Stockbridge, Mass., June 10-12. Dr. Charles C. Higgins, 2020 East 93d St., Cleveland, Secretary.
American College of Radiology, Chicago, June 6. Mr. Mac F. Cahal, 540 North Michigan Blvd., Chicago, Executive Secretary.
American Ophthalmological Society, Hot Springs, Va., June 10-12. Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y., Secretary.
American Society of Clinical Pathologists, Chicago, June 4-6. Dr. Alfred S. Giordano, 531 North Main St., South Bend, Ind., Secretary.
Montana, Medical Association of, Billings, July 7-8. Dr. Thomas F. Walker, 206 Medical Arts Building, Great Falls, Secretary.
Rhode Island Medical Society, Providence, June 2-3. Dr. William P. Buffum, 122 Waterman St., Providence, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1932 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Psychiatry, New York

99:475-632 (Jan.) 1943

Clinical Studies in Schizophrenia: Follow-Up Study of Small Group of Cases of Deterioration with Few Special Trends (Schizophrenic "Surrender"). C. M. Campbell, Boston.—p. 475.
Thirty Condemned Men. A. J. Rosanoff, Sacramento, Calif.—p. 484.
Methods of Estimating Capacity for Recovery in Patients with Manic Depressive and Schizophrenic Psychoses. E. F. Gildea and Evelyn B. Man, New Haven, Conn.—p. 496.
Clinical and Biologic Interrelations Between Schizophrenia and Epilepsy. P. H. Hoch. New York.—p. 507.
Follow-Up Study of Series of Patients Treated by Electrically Induced Convulsions and by Metrazol Convulsions. B. L. Pacella and S. E. Barrera, New York.—p. 513.
Consideration of Some Experiences with Electric Shock Treatment in Mental Diseases, with Special Regard to Various Psychosomatic Phenomena and to Certain Electrotechnical Factors. W. Sulzbach, K. J. Tillotson, V. Guillemin Jr. and G. F. Sutherland, Waverley, Mass.—p. 519.
Comparative Electroencephalographic Observations Following Electro Shock Therapy Using Raw 60 Cycle Alternating and Unidirectional Fluctuating Current. L. D. Proctor and J. E. Goodwin, Toronto, Canada.—p. 525.
Convulsive Shock Therapy in Elderly Patients: Risks and Results. V. L. Evans, Aurora, Ill.—p. 531.
*Study of Malnutrition in Chronic Schizophrenia. C. N. Baganz, Great Lakes, Ill., and J. M. Norris, Lyons, N. J.—p. 534.
Studies on Prognosis in Schizophrenia-like Psychoses in Children. R. S. Lourie, B. L. Pacella and Z. A. Piotrowski, New York.—p. 542.
Psychopathology of Aging. O. Diethelm and F. V. Rockwell, New York.—p. 553.
Treatment of Involutional Psychoses with Diethylstilbestrol. E. Davidoff, E. C. Reifenstein Jr. and G. L. Goodstone, Syracuse, N. Y.—p. 557.
Alcohol Detoxication Mechanism in Central Nervous System. J. G. Dewan, Toronto, Canada.—p. 565.
Disappointing Results with Bilateral Prefrontal Lobotomy in Chronic Schizophrenia. Gert Heilbrunn and P. Hletko, Chicago.—p. 569.
Psychotic Visitors to Government Offices in the National Capital. J. L. Hoffman, Washington, D. C.—p. 571.
Psychosomatic Interrelationship of Uterine Retrodisplacement and Prolapse to Normal and Psychotic Women. H. C. Leavitt, Kankakee, Ill.—p. 576.
Moonlight and Nervous Disorders: Historical Study. J. F. Oliven, Chicago.—p. 579.
Psychiatry as Social Science. G. Zilboorg, New York.—p. 585.
Review of Psychiatric Progress 1942: Military, Forensic and Administrative (?) Psychiatry. W. Overholser, Washington, D. C.; N. D. C. Lewis, New York; J. C. Whitehorn, Baltimore, with assistance of R. G. Hoskins, Boston; K. M. Bowman, San Francisco, with assistance of H. C. Solomon, Boston; J. Wortis, New York; W. G. Lennox, Boston; L. Kanner, Baltimore; F. G. Ebaugh and C. A. Rymer, Denver.—p. 589.

Malnutrition in Chronic Schizophrenia.—Baganz and Norris determined the extent and degree of the malnutrition of 374 schizophrenic patients on admission and after they had been hospitalized up to eight years. In their determination they considered the height, the age and the degree of activity of each patient. For comparison the nutrition of the total hospital population was studied. On admission the malnutrition of patients with chronic schizophrenia was not significantly different from that of the entire hospital population. However, while the entire hospital population changed little in the extent of malnutrition after admission there was a significant increase in the degree of malnutrition of the schizophrenic patients after eight years of hospitalization. The proportion of patients 10 or more pounds (4.5 Kg.) underweight was approximately 50 per cent greater among those with chronic schizophrenia studied than among the entire hospital population, and the same proportion was true of those with schizophrenia 20 or more pounds (9 Kg.) underweight. The more active patients appeared to have the lowest extent and degree of malnutrition. The extent and degree of malnutrition was apparently completely independent of the serving of an adequate caloric diet. The degree of malnutrition associated with chronic schizophrenia may offer an explanation for some of the common changes observed in the cardiac shadow and described as the "longitudinal heart of the precox."

American Journal of Surgery, New York

59:459-608 (March) 1943

Trends in Spinal Anesthesia. H. S. Ruth and D. D. Grove, Philadelphia.—p. 462.
Management of Retained Cervical Stump: Brief Analysis of 44 Cases. C. H. Tyrone and J. C. Weed, New Orleans.—p. 473.
*Influence of Estrogens on Genuine Preeclampsia and Eclampsia. E. Shute, London, Ont., Canada.—p. 478.
Acute Gastroduodenal Perforation. R. F. Barber and J. L. Madden, Brooklyn.—p. 484.
Snapping Hip. H. Dudgeon Jr., Waco, Texas.—p. 496.
Subastragaloid Arthrodesis for Os Calcis Type of Flatfoot. D. G. Leavitt, Seattle.—p. 501.
Well Thigh Traction in Treatment of Intertrochanteric Fractures. I. Stein and R. M. Lewis, Philadelphia.—p. 509.
Syndrome of Fixed Omentum. G. Ashworth, Philippi, W. Va.—p. 513.
Hernioplastic Operations on Rectum and Pelvic Floor. C. W. Barrett, Chicago.—p. 519.
Vesicointestinal Fistula—Actual and Incipient: Early Diagnosis and Treatment. J. A. Lazarus and M. S. Marks, New York.—p. 526.
Abscesses About the Anorectum. S. T. Ross, Hempstead, N. Y.—p. 536.
Symptomatic Pilonidal Cyst: Operative Treatment. M. N. Camp and N. Polites, Camp Polk, La.—p. 541.
Suspensory Muscle of Duodenum. J. C. Haley and J. K. Peden, Dallas, Texas.—p. 546.
Venography of Lower Extremity: New Technic—Preliminary Report. E. Zax, Houston, Texas.—p. 551.
Use of Sulfathiazole Vaseline Ointment. V. Mooney and F. A. Taylor, Pittsburgh.—p. 554.

Influence of Estrogens on Genuine Preeclampsia and Eclampsia.—Shute reports the use of estrogen in the treatment of eclampsia in 11 women. It is unfortunate that certain workers have, on this basis, begun to administer simultaneously prodigious doses of estrogens and progesterone, which are antagonistic substances. All of the author's preeclamptic patients remained ambulant. As estrogen is more effective in preeclampsia than in eclampsia, it should be used for prophylaxis rather than for therapy. Recognition of preeclampsia is the crux of the situation for which a blood estrogen assay is a sine qua non. Unless the assay method is used this therapeutic method will be discredited, for estrogens given to noneclamptic women may actually do harm, perhaps precipitate abruptio placentae.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

27:1-132 (Jan.) 1943

Chemotherapeutic Prophylaxis with Sulfonamide Drugs: I. Effect of Small Doses of Sulfathiazole or Sulfadiazine on Visual Efficiency. F. W. Reynolds, Mildred S. Evans and F. B. Walsh, Baltimore.—p. 2.
Reinfection in Syphilis: Newer Concept of Reinfection Encountered with Ten Day Arsenotherapy of Early Syphilis Controlled by Quantitative Serologic Tests. A. G. Schoch and L. J. Alexander, Dallas, Texas.—p. 15.
Experimental Prophylaxis of Chancroid Disease. R. B. Greenblatt, E. S. Sanderson, F. Mortara and H. S. Kupperman, Augusta, Ga.—p. 30.
Further Evidence Concerning Specificity of Lymphogranuloma Venereum Complement Fixation Test in Syphilis. A. W. Grace, New York; M. F. Shaffer and G. Rake, New Brunswick, N. J.—p. 44.
Evaluation of Yolk Sac Antigen for Frei Test: Comparison of Tests Performed with Antigens from Yolk Sac Cultures and from Human Pus. Helen Ollendorff Curth, New York.—p. 47.
Microscopic Pathologic Appearance of Aorta in Treated and Untreated Cases of Syphilitic Aortitis. E. G. Howe, New York.—p. 50.
*Methyl Glucamine Ascorbate (Ascorbic Acid Derivative) as a Solvent for Arsenical Drugs. H. Beerman, H. Pariser and Virgene Scherer Wammock, Philadelphia.—p. 58.
State Syphilis Consultation Program for Private Practitioners. M. M. Kroll, Albany, N. Y.—p. 63.
Syphilis in Industry. N. A. Nelson, Baltimore.—p. 73.
Syphilis and Elizabethan Playwrights and Pamphleteers. E. L. Zimmermann, Baltimore.—p. 78.

Methyl Glucamine Ascorbate as Solvent for Arsenical Drugs.—In the last two years Beerman, Pariser and Wammock have evaluated the value of a vitamin C solvent for arsenical drugs in 114 syphilitic patients who had reactions which necessitated the withdrawal of trivalent arsenicals. The solvent used contained methyl glucamine ascorbate equivalent to 60, 100 and 500 mg. of ascorbic acid in 10 cc. of a 7 per cent solution of

sucrose. This form of treatment definitely prevented a recurrence of the reaction in 58 per cent of the 114 patients, in 24.3 per cent the good effects that occurred could not with certainty be ascribed to the use of the solvent and in 17.7 per cent produced no appreciable effect in the prevention of nausea, vomiting and nitritoid crises. The solvent containing the 100 mg. dose was especially effective.

Annals of Surgery, Philadelphia

117:161-320 (Feb.) 1943

*Surgical Treatment of Tophaceous Gout. R. R. Linton and J. H. Talbott, Boston.—p. 161.

Total Gastrectomy for Cancer. F. de Amesti, Santiago, Chile.—p. 183.

Pilonidal Cyst: Local Use of Buffered Sulfanilamide in Primary Closure. J. V. Scott, Fort Belvoir, Va.—p. 191.

Biliary Dyskinesia from Surgical Viewpoint. J. E. Strode, Honolulu, Territory of Hawaii.—p. 198.

*Administration of Morphine and Antispasmodics in Biliary Colic. R. R. Best and J. H. Barr, Omaha.—p. 207.

Multilocular Serous Cysts of Round Ligament Simulating Incarcerated Hernias: Report of 3 Cases. D. Kershner and A. L. Shapiro, Brooklyn.—p. 216.

Acute Appendicitis During Later Decades of Life: Some Remarks on Incidence of Disease in Rural Area. J. H. Powers, Cooperstown, N. Y.—p. 221.

*Pathology of Burns: Pathologic Picture as Revealed at Autopsy in Series of 61 Fatal Cases Treated at Hospital for Sick Children, Toronto, Canada. I. H. Erb, Ethel M. Morgan and A. W. Farmer, Toronto, Canada.—p. 234.

Intra-Abdominal Use of Mikulicz Pack. T. E. Jones, J. R. Paxton and R. E. Brubaker, Cleveland.—p. 256.

Reduction of Mortality in Surgical Management of Hyperthyroidism: Use of Short Interval Two Stage Lobectomy. W. C. Sealy and H. B. Kernodle, Durham, N. C.—p. 263.

Echinococcus Cyst of Lung Exhibiting Unusual Radiologic and Surgical Features. C. D. Benson, W. A. Evans Jr. and W. W. Zuelzer, Detroit.—p. 268.

Evolution of Spinal Fusion. M. B. Howorth, New York.—p. 278.

Stenosing Tendovaginitis at Radial Styloid (de Quervain's Disease). P. C. Potter, New York.—p. 290.

Trends in General Surgery: Review of Five Years Surgical Experience at Harper Hospital. M. J. Thorstad, H. C. Saltzstein and A. D. McAlpine, Detroit.—p. 297.

Surgical Treatment of Tophaceous Gout.—Linton and Talbott base their report on the surgical treatment of the tophaceous gout of 10 men and 1 woman from 20 to 80 years of age; 8 of them were more than 50, 2 were in their twenties and 1 was in the ninth decade. Seven of the patients had had their gout for twenty or more years, 2 for ten to twenty years and 2 for seven years. The surgical treatment of gout is applicable only to patients in whom large tophaceous deposits have developed. Surgery on the 11 patients was limited to the removal of urate deposits which involved the bony and soft structures about the elbows, forearms, wrists, hands and feet. The indications for surgical treatment are cosmetic reasons, pain, interference with movements, discharging sinus and extensive phalangeal involvement of the fingers or toes. Forty-six operative procedures were undertaken on the 11 patients. An analysis of the lesions revealed thirty-one subcutaneous tophi, thirty-six involving tendons and adjacent structures and twenty-six which arose from joints with invasion of bone and soft tissue. Of the ninety-three tophaceous deposits operated on only approximately 5 per cent occurred at the great toe. The surgical procedures on the hands were and should, of necessity, be more conservative than those on the feet. Follow-up studies six months or more postoperatively or to the death of the patient showed that in only three out of the ninety-three tophaceous deposits were there recurrences of any size; one was in the finger of a woman with extensive deposits, one was a recurrence of tophus in the flexor tendon in the palm because removal had been incomplete and one of the finger was among the earlier operations in which complete removal of the tophaceous deposit had not been obtained. Relief from pain followed the surgical removal of the tophaceous deposits in all the patients; 4 patients with extensive involvement of the feet, who were unable to walk or could walk only with extreme pain, were rehabilitated so that they could get about without pain. The 8 patients who had painful tophi removed from the hands and fingers obtained decided relief of symptoms and considerable functional restoration. Since good results are possible by the surgical removal of tophaceous deposits, even late in life, it is recommended that surgery be done earlier in the course of the disease than usually is considered desirable.

Morphine and Antispasmodics in Biliary Colic.—Best and Barr carried out a series of experiments on the problem of relieving biliary colic. An antispasmodic drug which would consistently relax the wall of the gallbladder, the region of the cystic duct and the sphincter area at the lower end of the common duct would not only hasten and prolong the relief obtained by the necessary morphine but might also prevent further extension of the pathologic process by permitting free drainage of the biliary tract. With an intact gallbladder, biliary pain is most frequently due to increasing pressure within the gallbladder. With a pathologic gallbladder, the choledochal sphincter may or may not be in a spastic state, causing increased pressure in the biliary ducts which would also contribute to the pain. Atropine could be indicated, as at times it definitely relaxes the sphincter area or at least raises its threshold of irritability. Since this spastic state of the choledochal sphincter may be contributing to pain accompanying the gallbladder colic, morphine hypodermically and glyceryl trinitrate orally should be tried thirty minutes to a few hours later if the morphine-atropine combination has not given relief. Either atropine or glyceryl trinitrate should be given with morphine to help counteract the tone or spasm stimulating effect of the morphine on intrabiliary pressure. For patients who have had a previous cholecystectomy the morphine and glyceryl trinitrate combination should be tried first for biliary colic and if it does not afford relief a morphine-atropine injection should be given. Probably the morphine-atropine combination should be tried first for patients with an intact gallbladder and then the atropine with glyceryl trinitrate alternately every four hours. Morphine should be used in the four intervals only as needed. This may be continued for several days in the hope that the cystic duct will become sufficiently relaxed to permit egress of thick bile from the gallbladder into the common duct and then the sphincter of Oddi would be sufficiently relaxed to permit the bile to pass into the duodenum. When the gallbladder has been removed, the morphine-glyceryl trinitrate combination is most apt to give relief. The glyceryl trinitrate is then alternated with atropine every four hours for several days and morphine is added as necessary.

Pathology of Burns.—Erb and his associates discuss pathologic changes in 61 fatal burn cases. Tannic acid was used in 41 and was not used in 20. The more important changes remote from the burned area involved liver, kidney, gastrointestinal tract and adrenal, with infection of one sort or another superadded. Duodenal ulcer was observed in 5, esophagitis or esophageal ulceration in 5, early gastric ulcer in 3 and adrenal hemorrhage in 4. Of the 41 patients whose burns were tanned, 25 presented hepatic necrosis. The shortest time that a patient survived after the burn in whom necrosis was found was sixty hours, the longest was nineteen days; 17 died within three to five days. Death up to the fifth day was attributed to toxemia and thereafter to infection. Signs of hepatic repair were noted in each of 5 patients who died between the eighth and the nineteenth day. Of 27 patients dying within three to nineteen days only 3 were free from hepatic necrosis. Hepatic necrosis did not occur in any of the group whose wounds were not tanned, 7 of whom died within three to fourteen days. Renal damage was observed in 19, and for all but the burn of 1 tannic acid was used. Following the introduction of tannic acid in 1925, the mortality rate from burns fell from 35.2 to 11.8 per cent and after the use of sulfonamides and other measures it fell to 2.9 per cent. Also with the introduction of tannic acid the time of death shifted from the first twelve to thirty-six hours to the period of toxemia, the third to the sixth day, the period in which hepatic necrosis is most frequently observed. Patients dying with hepatic necrosis, apart from those dying of sepsis, presented, on the whole, the same clinical picture of toxemia as did those without hepatic necrosis for whom tannic acid was not used and who died during the same period. Therefore hepatic necrosis, whatever its cause, is not necessarily the cause of death, although it may be a serious complication. Some therapeutic agent to be used with tannic acid should be sought which would preserve the benefits of tannic acid and at the same time protect the liver from the necrosis resulting from the absorption of a toxic substance from the burned skin and/or the direct or indirect result of tannic acid.

Archives of Pathology, Chicago

35:357-502 (March) 1943

*Metastasis of Mixed Tumors of Salivary Glands. R. M. Mulligan, Denver.—p. 357.
*Commercial Lead as Possible Inciting Factor in Bronchiogenic Carcinoma: Report of 2 Cases. C. E. Black, East Lansing, Mich.—p. 366.
Morphologic Changes in Rat's Adrenal Cortex Under Various Experimental Conditions. E. L. Sarason, New York.—p. 373.
Parvilocular Tumors of Ovary. W. Schiller, Chicago.—p. 391.
Fialarial Epididymofuniculitis. J. G. Pasternack, Staten Island, N. Y. p. 414.
Blood Cholesterol. S. Weinhouse, Chicago.—p. 438.

Metastasis of Mixed Tumors of Salivary Glands.—Mulligan's review of the localization of the metastases of 20 previously reported cases and 1 of his own shows that metastases were present in the lungs of 18, the pleurae of 12, the liver of 10, the bones of 8, the lymph nodes of 6, the kidneys of 3 and the spleen of 2. The term "cylindroma" was employed in the microscopic description of the tumor of 8. In 4 others, from the description given, this same appearance was present. In 5 the designation was "mixed tumor," in 2 "adenocarcinoma" and in 2 "malignant glandular epithelioma" and "alveolar sarcoma." The data suggest that when a patient in the fourth to the seventh decade of life has a tumor of a salivary gland a thorough examination must rule out metastasis if operation or irradiation of the primary tumor is contemplated.

Lead and Bronchiogenic Carcinoma.—Lead and radium belong to the same chemical family. As commercial lead contains varying amounts of radioactive substances, usually radium D, it should be considered as a possible inciting factor in bronchiogenic carcinoma when its dust and fumes are inhaled over long periods. In the 2 cases that Black presents there was continuous exposure to lead for many years. That carcinoma may not manifest itself until many years after exposure to irritating dusts was borne out by the cases. The first patient had recurrent attacks of lead intoxication and an amount of lead in the urine indicating that lead was actually taken into the body. At necropsy chronic fibroid pneumonitis was found in both patients, suggesting some form of chronic irritation.

Arkansas Medical Society Journal, Fort Smith

39:193-212 (Feb.) 1943

Common Head Injuries. E. M. Miers, Mena.—p. 193.

39:213-228 (March) 1943

Hypertension: Newer Theories, Prognosis and Treatment. J. N. Compton, Little Rock.—p. 213.

Bulletin of Johns Hopkins Hospital, Baltimore

72:1-64 (Jan.) 1943

Pyridoxine Deficiency in Swine, with Particular Reference to Anemia, Epileptiform Convulsions and Fatty Liver. M. M. Wintrobe, R. H. Follis Jr., M. H. Miller, H. J. Stein, R. Alcayaga, S. Humphreys, A. Suksta and G. E. Cartwright, Baltimore.—p. 1.
Hormone Production by Placental Cells Maintained in Continuous Culture. G. E. S. Jones, G. O. Gey and M. K. Gey, Baltimore.—p. 26.
Effect of Purified Diet Deficient in Carbohydrate on Rat. R. H. Follis Jr. and W. M. Straight, Baltimore.—p. 39.
*Sulfanilamide as Prophylactic Agent in Rheumatic Fever. Caroline A. Chandler and Helen B. Taussig, Baltimore.—p. 42.
Study of Thoracic Duct Lymph in Experimental Crush Injury and Injury Produced by Gross Trauma. A. Blalock, Baltimore.—p. 54.

Sulfanilamide as Prophylactic in Rheumatic Fever.—Chandler and Taussig state that in the 16 patients to whom they gave sulfanilamide as a prophylactic for two seasons and in the 9 so treated for one season (forty-one "patient seasons"), a questionable recurrence of rheumatic fever occurred in only 1. In a comparable group of control patients, 17 observed for two seasons and 7 for one season, there were five recurrences. Studies of the beta hemolytic streptococci isolated from the patients' throats permit no conclusions, but they do suggest that an investigation might be undertaken on a larger series of patients. In the sulfanilamide group 3 patients harbored group A streptococci for considerable periods of time. Antibodies were present for prolonged periods in 2 of the 3. Homologous antibodies were also present in 2 patients who harbored group C organisms for some time. In the control group 7 patients had streptococci at some time; the organisms were isolated only once in each of them.

Bulletin New York Academy of Medicine, New York

19:77-150 (Feb.) 1943

Gallbladder Disease: Etiology, Diagnosis and Treatment. T. H. Russell, R. F. Carter and E. Oppenheim, New York.—p. 77.
Diagnosis and Prognosis of Brain Tumors. G. Horrax, Boston.—p. 125.
Some Recent Advances in Therapeutics, Including Newer Drugs of Sulfonamide Group. H. Gold, New York.—p. 132.

Canadian Journal of Public Health, Toronto

34:51-96 (Feb.) 1943

Health Problems in National Defense Areas. A. R. Morton, Halifax, N. S.—p. 51.
Nutritional Planning. L. B. Pett, Ottawa, Ont.—p. 58.
Growing Recognition of Public Health and Preventive Medicine. A. Plouffe, Montreal.—p. 63.
Study of Effect of Fixed Pace Work on Health. G. H. Turner, Ottawa, Ont.—p. 68.
Health Education—Through the Drug Store Window. H. C. Rhodes, Vancouver, B. C.—p. 74.
The Sanitary Inspector and Public Relations. M. F. Matthews, Toronto.—p. 79.

Canadian Medical Association Journal, Montreal

48:93-190 (Feb.) 1943

Incidence of Catarrhal Jaundice Compared with Jaundice Following Arsenotherapy for Syphilis. H. S. Mitchell.—p. 94.
Activities of the Royal Canadian Navy Medical Research Unit. C. H. Best and D. Y. Solandt, Toronto.—p. 96.
Elementary Principles of Treatment of Head Injuries. W. Penfield and W. Cone, Montreal.—p. 99.
*Analysis of Pneumonia Deaths Since Introduction of Sulfonamide Therapy. J. C. Meakins and R. D. McKenna, Montreal.—p. 104.
Problem of Functional Disease as Seen in Industry. D. E. Bell, Toronto.—p. 108.
Thyrotoxicosis and Its Treatment. W. R. Campbell, Toronto.—p. 110
Accuracy of Tests for Syphilis, with Particular Reference to Laughlen Method. G. F. Laughlen, Toronto.—p. 114.
Memorandum on Possible Methods for Prevention of Rheumatic Manifestations in the Armed Forces. R. Hare, Toronto.—p. 116.
Diffusion of Sulfonamides Out of Certain Bases. R. A. Waud and A. Ramsay, London, Ont.—p. 121.
Expectorant Action of Creosote and Guaiacols. Mary E. Stevens, Alice K. Ronan, T. S. Sourkes and E. M. Boyd, Kingston, Ont.—p. 124.
Exfoliative Dermatitis. K. A. Baird, West Saint John, N. B.—p. 128.
Mortality and Morbidity Following Operations in a General Hospital. D. C. Aikenhead and Evelyn Gamble, Winnipeg, Man.—p. 129.
Second Year Anemias. E. Cairns, Lethbridge, Alta.—p. 132.

Analysis of Pneumonia Deaths.—Meakins and McKenna analyze 21 fatal cases of (pneumococcic) lobar pneumonia treated in the Royal Victoria Hospital during three years. All deaths occurred from infections with the lower types (through XIV) of pneumococci. The mortality rate of 10.5 per cent (21 of 200 cases) was comparable with that of most figures. The sex incidence of mortality was exactly proportional to that of the incidence of the disease, 3 males to 1 female. All deaths except those of 2 infants were of persons more than 40; the average age of the patients who died was 56.3 years and that of the survivors was 36.1. The mortality rate among type III infection was disproportionately high (23.5 per cent). At least 10 of the patients who died had bacteremia. Malnutrition or associated disease (involving the cardiovascular system, lungs, kidneys, liver or sinuses) was present in more than 90 per cent of the patients who died and in only 29 to 32 per cent of the survivors. It is suggested that the recognition of nonspecific factors, both in the determination of the prognosis and in the management of the disease, would further lower the mortality rate from pneumococcic lobar pneumonia.

Connecticut State Medical Journal, Hartford

7:149-222 (March) 1943

Social Functions of the Modern Hospital. G. M. Mackenzie, Cooperstown, N. Y.—p. 151.
Rheumatic Fever in United States: Its Public Health Implications. L. Spekter, Hartford.—p. 156.
Treatment of Acute Attack of Asthma. J. Weiner, New Haven.—p. 164.
Radioresistant Cancer of Upper Lip: Case Report. E. T. Bradley, New Canaan.—p. 166.
Leiomyoma of Small Intestine: Case Report. D. C. Patterson and W. A. Geer, Bridgeport.—p. 168.
Osteochondritis Dissecans of Elbow Joint with Unusual Approach for Removal of Loose Body. E. H. Crosby, Hartford.—p. 170.
Tumor of Carotid Gland. G. H. Twombly, New York; L. G. Simon and L. Steinberger, South Norwalk.—p. 172.
Prelude to Surgical Anesthesia. A. H. Miller, Providence, R. I.—p. 176.

Florida Medical Association Journal, Jacksonville

29:345-392 (Feb.) 1943

Arterial Hypertension. W. Merritt, Jacksonville.—p. 357.
Pyuria in Childhood: Its Significance and Treatment. W. W. Quillian, Coral Gables.—p. 361.
Modern Diagnostic Procedures in Syphilis. L. C. Gonzalez, Tampa. —p. 364.
Preoperative and Postoperative Management of Hypertrophic Pyloric Stenosis: Review of 40 Cases. N. Weil Jr., Jacksonville.—p. 369.
Glomus Tumor: Report of Case. M. J. Loeb, Miami Beach.—p. 372.
Acute Urinary Suppression Following Sulfadiazine Therapy. C. F. Roche, L. W. Elgin and D. G. Stannus, Miami Beach.—p. 374.

Gastroenterology, Baltimore

1:1-132 (Jan.) 1943

Prepyloric Lesions of Stomach: Medical and Surgical Aspects. Sara M. Jordan and F. H. Lahey, Boston.—p. 1.
Known and Unknowns in Problem of Optimal Nutrition. A. J. Carlson, Chicago.—p. 13.
Correlation of Cytologic with Chemical Changes in Liver as Influenced by Diet, Particularly Protein. R. Elman, Margaret G. Smith and L. A. Sachar, St. Louis.—p. 24.
The Coated Tongue. B. R. Crohn and R. Drosd, New York.—p. 34.
Chronic Epigastric Distress and Its Role in Chronic Gastritis: Analysis of the Problem. R. Schindler, Chicago.—p. 44.
Chronic Nonspecific Gastritis: Significance as Clinical Entity. G. B. Eusterman, Rochester, Minn.—p. 54.
*Hypertrophic Gastritis: Gastroscopic and Clinical Studies. E. B. Benedict, Boston.—p. 62.
Gastroscopic Study of Healthy Individuals: Preliminary Report. J. H. FitzGibbon and G. B. Long, Portland, Ore.—p. 67.
*Relationship of Concentration of Proteins in Serum to Postoperative Gastric Retention. L. R. Chauncey and H. K. Gray, Rochester, Minn.—p. 72.
The Irritable Digestive Tract. W. C. Alvarez, Rochester, Minn.—p. 95.
Effect of Antacid Therapy on Peptic Activity of Gastric Juice in Man. I. A. Warren, J. Front and J. B. Kirsner, Chicago.—p. 102.

Hypertrophic Gastritis.—Benedict applies the term hypertrophic gastritis to the finding on gastroscopy of numerous verrucous elevations in the gastric mucosa, beading or caterpillar-like appearance of the rugae and dulness or diminished highlights in the mucosa. Among 1,300 gastroscopies he diagnosed hypertrophic gastritis without other gastric or duodenal pathologic changes in 117 (9 per cent). Of the total, 61 per cent were in males. The disease rarely occurs before 20 or after 70. The symptoms of hypertrophic gastritis in the order of their frequency are epigastric pain, vomiting, gas, sour eructations, heartburn and nausea without vomiting. There is no specific treatment. Of the 92 patients 26 were relieved by a bland diet alone and 72 by a bland diet with or without belladonna, alkaline powders, aluminum hydroxide, hydrochloric acid or liver therapy. Nine patients were not relieved by diet, 2 were not relieved by alkaline powders, 1 was not relieved by belladonna and of 5 operated on 3 were relieved. The improvement seen at subsequent gastroscopy was definitely correlated with the clinical improvement in most instances. The expert roentgenologist using the relief technic may be helpful in suggesting a possible diagnosis of gastritis, but only gastroscopy permits a positive diagnosis or differential diagnosis between the superficial, atrophic and hypertrophic forms. In differentiating some severe and doubtful cases of hypertrophic gastritis from carcinoma, gastrotomy and biopsy should be performed.

Proteins in Serum and Postoperative Gastric Retention.—Chauncey and Gray estimated the concentration of protein in the serum of patients during the normal postoperative period of various surgical procedures on the upper portion of the gastrointestinal tract. There was a normal decline in the concentration of the total proteins and a decline in the concentration of the two fractions; the decline of the albumin fraction was slightly more pronounced than that of the globulin fraction. After the fifth postoperative day there was a steady and persistent increase in the concentration of total proteins and the albumin and globulin fractions. A concentration of less than 5.2 Gm. of total protein per hundred cubic centimeters occurred frequently without gastric retention. Concentrations of less than 3 Gm. of albumin per hundred cubic centimeters never were observed. Regeneration of globulin was not rapid. Estimations of the concentration of serum protein, the two fractions and the colloidal osmotic pressure of 15 patients after operations on the stomach whose postoperative course was marred by postoperative gastric retention revealed that gastric retention was associated with a concentration of serum protein within normal limits or within normal postoperative limits. Gastric retention was associated with a colloidal osmotic pressure well in excess of the "critical edema level" (160 to 200 mm. of water). The amount of retention was not paralleled by fluctuations in the concentration of serum proteins or the albumin fraction of the colloidal osmotic pressure. Retention frequently diminished and disappeared with a coincidental decrease in serum osmotic pressure and in the concentration of serum proteins. Clinical edema caused by hypoproteinemia was noticed postoperatively at the same time at which gastric retention disappeared.

Georgia Medical Association Journal, Atlanta

32:33-64 (Feb.) 1943

Care of Premature Infants. W. W. Anderson, Atlanta.—p. 33.
Medical Ethics. J. W. Simmons, Brunswick.—p. 37.
Functional Digestive Disease as Seen at Lawson General Hospital. D. T. Chamberlin.—p. 40.
The Arthritic Problem at Lawson General Hospital. J. J. Wallace.—p. 43.
Paroxysmal Tachycardia of Young Infants: Report of Case. L. M. Blackford and L. D. Hoppe, Atlanta.—p. 47.
Encephalomyelitis Following Smallpox Vaccination: Report of Case. R. L. Rogers and W. H. Hill, Gainesville.—p. 48.

Illinois Medical Journal, Chicago

83:77-144 (Feb.) 1943

Fetal Distress During Labor. C. J. Lund, Madison, Wis.—p. 96.
Respiratory Disturbances in Newly Born Infant. Edith L. Potter, Chicago.—p. 100.
Prostigmine Pregnancy Test and Treatment for Delayed Menstruation. M. J. Sneider, Chicago.—p. 107.
Conservative Management of Sinuses. L. T. Curry, Chicago.—p. 111.
Hypochromic Anemia and Malignancy. H. Swanberg, Quincy.—p. 116.
Jaundice Associated with Giardia Lamblia Infestation. C. H. Drenckhahn, Urbana.—p. 119.
Atypical Problems in Appendicitis. J. E. Bellas and D. V. Auld, Peoria.—p. 121.
Report of 2 Cases of Glycogen Storage Disease in Two Members of One Family. L. T. Gregory, J. B. Gillespie, Urbana, and R. C. Armstrong, Champaign.—p. 123.
Acute Psychosis in Selectees. S. D. Klow, Elgin.—p. 125.
Occult Blood in Stool. C. J. Drueck, Chicago.—p. 130.
Mumps with Edema of Chest. J. N. Rappaport, Evanston.—p. 133.

Indiana State Medical Assn. Journal, Indianapolis

36:123-180 (March) 1943

Effective War Participation. W. F. Donaldson, Pittsburgh.—p. 123.
Industrial Health and the War. C. M. Peterson, Chicago.—p. 125.
Army Air Corps' New Convalescent Program. H. A. Rusk, Jefferson Barracks, Mo.—p. 127.
Psychologic and Sociologic Background of the Criminal. C. R. Bird, Indianapolis.—p. 128.
Report of Experiences with Demerol: New Departure in Analgesia. R. Hoffman, South Bend.—p. 135.
Influenza and Pneumonia in Indiana. J. W. Jackson, Indianapolis.—p. 137.
Allergy in Hearing Defects. H. A. Kuhn, Hammond.—p. 143.
Unusual Intranasal Tumor. B. E. Ellis, Indianapolis.—p. 147.

Iowa State Medical Society Journal, Des Moines

33:89-146 (March) 1943

*Observations on Treatment of Diabetes Mellitus. W. H. Olmsted, St. Louis.—p. 95.
Diphtheria Prevention. J. E. Dyson, Des Moines.—p. 101.
Immunization Procedures for Smallpox and Scarlet Fever. A. M. Smythe, Des Moines.—p. 102.
Active Immunization for Pertussis. Charlotte Fisk, Des Moines.—p. 103.
Active Immunization Against Tetanus. L. F. Hill, Des Moines.—p. 105.
Prophylactic Procedures for Certain Communicable Diseases. C. F. Jordan, Des Moines.—p. 107.
Mycotic Pulmonary Infections: Report of Case. W. M. Block, Cedar Rapids.—p. 108.
Pernicious Anemia: Report of Case with Fifteen Year Remission. A. L. Jenks Jr., Des Moines.—p. 112.

Observations on Treatment of Diabetes Mellitus.—Olmsted believes that if the diabetic patient receives a diet which fulfils the caloric, mineral and vitamin requirements and if he is kept sugar free and the obese diabetic patient reduces, the premature development of arteriosclerosis will be prevented and the patient will live approximately as long as any one else. His experience with protamine zinc insulins which contain less protamine leads him to believe that they are better adapted to the treatment of the disease than the forms of protamine zinc insulin now in use. The success of the dietetic management of

the diabetic patient depends a great deal on dietetic education and simple methods. Use of the measuring cup results in better control of the diet than the use of the metric system in spite of its undoubted accuracy.

Journal of Immunology, Baltimore

46:1-46 (Jan.) 1943

Neutralization Tests with Fractions of Poliomyelitis Antiserum (Horse). J. A. Toomey, Cleveland; C. F. McKhann, Ann Arbor, Mich., and Kathleen Fahey, Boston.—p. 1.
Preparation and Use of Rh Testing Serums. F. W. Gallagher and L. R. Jones, St. Louis.—p. 9.
Progress in Study of Bacillary Dysentery. A. J. Weil, Pearl River, N. Y.—p. 13.

Journal-Lancet, Minneapolis

63:1-30 (Jan.) 1943

*Wounds of Heart: Review of Seventeen Cases with Four Operations. H. M. Blegen, Missoula, Mont.—p. 1.
Emergency Treatment of Lacerations. V. G. Borland, Fargo, N. D. —p. 8.
The Depressed Patient. G. R. Kamman, St. Paul.—p. 11.
Fifty Years of Students' Health Work. R. T. Legge, Berkeley, Calif. —p. 16.
Psoriasis of Nails Producing an Arthritis-like Picture: Report of Case with Seven Year Follow-Up. L. C. Kelly, New York.—p. 19.
Relief of Colonic Obstruction. H. W. Christianson, Minneapolis. —p. 21.
Medical Aspects of Dental Health in Childhood. E. S. Platou, Minneapolis.—p. 22.

63:31-58 (Feb.) 1943

Coronary Insufficiency Precipitated by Hemorrhage from Duodenal Ulcer. C. A. McKinlay, Minneapolis.—p. 31.
Glaucoma and the General Practitioner. G. M. Constans, Bismarck, N. D.—p. 35.
Nutrition Problems Among College Students. J. J. Boehrer, Minneapolis. —p. 40.
Orthopedic and Medical Management of Arthritis: Preliminary Report. D. H. Levinthal and Catharine E. Logan, Chicago.—p. 48.
Cause of Toxemias of Pregnancy. R. T. LaVake, Minneapolis.—p. 51.
Report on Health Achievements in North Dakota. F. J. Hill, Bismarck, N. D.—p. 53.

Wounds of Heart.—Blegen thinks that in many hospitals the signs and symptoms of cardiac tamponade from injury is still unrecognized and that the patient presenting himself with the typical syndrome is often given up as beyond medical aid. Of 17 such patients admitted to St. Joseph Hospital during the last fourteen years 13 were Negroes and 4 were white. The wounds of 9 were due to gunshot, of 5 to stabs and 2 to nonpenetrating body blows. In 7 cardiac tamponade was proved at operation or necropsy. Four of these patients were operated on; 2 recovered. Five patients died in the emergency room before treatment could be given. Surgery was not offered to 6 in spite of the fact that they lived longer than one hour and 1 recovered with conservative measures alone. One of the 2 patients who had a cardiac injury, proved at necropsy as the result of nonpenetrating body blows, had a cardiac tamponade as a result of a rupture of the right auricle and lived five hours after admission. The other patient had a ruptured auricular endocardium which was not detected clinically but which would have been compatible with life had he not died from an accompanying gas bacillus infection. As cardiac rupture with tamponade following a body blow may be relieved surgically, all patients, especially those injured in automobile accidents, who show signs of cardiovascular collapse out of proportion to blood loss or other injuries should be examined carefully for tamponade with the hope of saving some of them by early operation.

Journal Neuropath. and Exper. Neurology, Baltimore

2:1-102 (Jan.) 1943

Calcified Epileptogenic Lesions as Caused by Incomplete Interference with Blood Supply of Diseased Areas. L. Alexander and B. Woodhall, Durham, N. C.—p. 1.
Experimental Intracranial Epithelial Cysts. A. Weil and B. Blumkoltz, Chicago.—p. 34.
Postmotor Foci Influencing Gastrointestinal Tract and Their Descending Pathways. E. A. Spiegel, K. Weston and M. J. Oppenheimer, Philadelphia.—p. 45.
Nuclei of Cranial Nerves in Human Case of Cyclopia and Arhinia. O. Marburg and F. A. Mettler, New York.—p. 54.
Pathologic Changes in Brain of Case Clinically Diagnosed Dementia Precox. A. Ferraro, New York.—p. 84.
New Staining Method to Demonstrate Pathogenic Yeasts and Fungi. J. W. Kernohan, Rochester, Minn.—p. 95.
Modification of Horsley-Clarke Stereotaxic Apparatus. P. Bailey and E. W. Davis, Chicago.—p. 99.

Journal of Nutrition, Philadelphia

25:1-102 (Jan.) 1943. **Partial Index**

Thiamine, Riboflavin, Pyridoxine and Pantothenate Deficiencies as Affecting the Body Composition of Albino Rat. L. Voris and H. P. Moore, Philadelphia.—p. 7.
Short Method of Calculating Nutritive Value of Diets. G. H. Berryman and Charlotte Chatfield, Washington, D. C.—p. 23.
Utilization for Hemoglobin Regeneration of Iron in Salts Used in Enrichment of Flour and Bread. F. I. Nakamura and H. H. Mitchell, Urbana, Ill.—p. 39.
Factors Affecting Thiamine Content of Breast Milk. Elizabeth M. Knott, Sarah C. Kleiger and F. Torres-Brachamonte, Chicago.—p. 49.
Disappearance of Cellulose and Hemicellulose from Digestive Tracts of Children. Frances Cope Hummel, Marion L. Shepherd and Icie G. Macy, Detroit.—p. 59.
Minimal Daily Requirement of Thiamine of Man. R. D. Williams, H. L. Mason and R. M. Wilder, Rochester, Minn.—p. 71.

Journal of Pediatrics, St. Louis

22:135-258 (Feb.) 1943

Effect of Infra-Red Heat on Localized Poliomyelitis and Neuritis. J. A. Toomey, Cleveland.—p. 135.
*Nonspecific Therapy in Anterior Poliomyelitis: Preliminary Report on Use of Vitamins B and E and Artificial Fever. S. Stone, Manchester, N. H.—p. 142.
Anthropometry in Pediatrician's Office: Norms for Selected Body Measurements Based on Studies of Children of North European Stock. Vernette S. Vickers and H. C. Stuart, Boston.—p. 155.
Rh Factor in Relation to Jaundice of Newborn Infant (Erythroblastosis Fetalis). F. W. Gallagher, P. G. Danis and L. R. Jones, St. Louis. —p. 171.
Cryptorchism. J. H. Lapin, W. Klein and A. Goldman, New York. —p. 175.
Colostrum as Source of Diphtheria Antitoxin in Actively Immunized Pregnant Mothers. J. Liebling and H. E. Schmitz, Chicago.—p. 189.
Exercise Tolerance Test as Measure of Chronic Fatigue in Children. R. E. Netzley, Pasadena, Calif.—p. 194.
Acute Febrile Illness with Rash and Leukopenia Due to Hemophilus Parainfluenzae. A. L. Florman, New York.—p. 202.
Low Carbon Dioxide Content as Prodrome of Diarrhea in Newborn Infant. J. W. St. Geme, Los Angeles.—p. 205.
Assessing Physical Condition of Children: II. Simple Malnutrition: Problem of Failing Growth and Development. N. C. Wetzel, Cleveland.—p. 208.
Purpura Fulminans (Waterhouse-Friderichsen Sundrome): Report of Case with Recovery. W. L. Rucks and J. J. Hobson, Memphis, Tenn.—p. 226.
Perforation of Ileum in Newborn Infant with Operation and Recovery: Case. H. A. Agerty, A. J. Ziserman and C. L. Shollenberger, Philadelphia.—p. 233.
Pretonsillectomy Clinic. B. S. Denzer and Gertrude Felshin, New York.—p. 239.

Nonspecific Therapy in Anterior Poliomyelitis.—Stone used artificial fever and vitamins B and E as found in wheat germ oil in the treatment of the acute and subacute anterior poliomyelitis of 12 patients; 6 also received artificial fever. In none of the patients treated—all except 1 had paralyses of varying degrees of severity—did any deformities or contractures develop. Muscle tenderness was greatly diminished in all, especially in those who received artificial fever and vitamin medication. The intravenous or intramuscular administration of thiamine hydrochloride during the acute stage appeared to exert a nonspecific beneficial influence on the patients' general condition and to lessen the severity of paresthesia. It was most effective when combined with artificial fever and given during the height of the fever. Vitamin E appeared to lessen the tendency to the development of fibrositis, increased muscle tone in chronic patients and possibly favorably influenced muscle regeneration when the nerve supply was not destroyed completely. Artificial fever therapy at 102 to 105 F. was well tolerated by all patients. It helped to reduce muscle tenderness, relieved vasospasm and muscle spasm, and improved the circulation of the spinal cord and brain by increasing the supply of oxygen to the central nervous system, thus improving the nutrition of the neurons not already destroyed. When combined with vitamins B and E it rapidly improved the symptoms in patients with progressive fibrositis. While vitamins B and E and artificial fever are nonspecific in their mode of action, they probably assist in the regeneration of the neurons partially affected by the virus, improve the patient's general condition and assist in preventing excessive fibrosis, a frequent cause of deformities and contractures.

Journal Pharmacology & Exper. Therap., Baltimore

77:107-206 (Feb.) 1943. **Partial Index**

Pharmacology of N-Substituted Carbamino Cholines. M. B. Bender, M. A. Spirtes and D. B. Sprinson, New York.—p. 107.
Sulfamethazine (2 - 4' - Aminobenzenesulfonylamino - 4: 6-Dimethylpyrimidine): New Heterocyclic Derivative of Sulfanilamide. F. L. Rose, A. R. Martin and H. G. L. Bevan, Manchester, England.—p. 127.
Noble-Collip Shock: Therapeutic Effects with Autonomic Depressants: Motion Factors. P. A. Zahl, S. H. Hutner and F. S. Cooper, New York.—p. 143.
Effect of Sodium Citrate Administration on Excretion of Lead in Urine and Feces. T. V. Letonoff and S. S. Kety, Philadelphia.—p. 151.
Studies on Sulfonamide Resistant Organisms: III. Origin of Sulfonamide Resistant Pneumococci. L. H. Schmidt and Clara L. Sesler.—p. 165.
Metabolism of Hydantoin Derivatives Closely Related to Dilantin. C. H. Hine and F. L. Kozelka, Madison, Wis.—p. 180.
Analgesic Properties of Certain Drugs and Drug Combinations. D. L. Smith, Marie C. D'Amour and F. E. D'Amour, Denver.—p. 184.
Toxicity of Acetoin. L. A. Greenberg, New Haven, Conn.—p. 194.

Journal of Thoracic Surgery, St. Louis

12:209-304 (Feb.) 1943

Surgical Approach for Incision and Drainage of Nonpurulent and Purulent Pericardial Effusions. J. K. Donaldson, Little Rock, Ark.—p. 209.
Management of Pulmonary Tuberculosis Complicated by Bronchial Tuberculosis, with Special Reference to Use of Artificial Pneumothorax. T. N. Rafferty and D. O. Shields, Northville, Mich.—p. 225.
Artificial Pleurodesis in Relation to Pulmonary Lobectomy. F. J. S. Gowar, London, England.—p. 234.
Primary Neurogenic Tumors of Mediastinum. V. D. Schaffner, Kentville, N. S., Canada; R. P. Smith and H. E. Taylor, Halifax, N. S., Canada.—p. 247.
Basal Tuberculosis. J. B. Andosca and J. A. Foley, Boston.—p. 259.
Principles Involved in Surgical Treatment of Diaphragmatic Hernias in Children. J. M. Dorsey, Chicago.—p. 267.
Chronic Fibrous Mediastinitis with Obstruction of Superior Vena Cava. Jane Erganian and L. J. Wade, St. Louis.—p. 275.
Tuberculous Endobronchitis and Upper Lobe Bronchiectasis. A. H. Aufses, New York.—p. 285.
Analysis of 150 Cases of Thoracoplasty for Tuberculosis at Bellevue Hospital. A. W. Harrison and F. B. Berry, New York.—p. 292.
Hodgkin's Disease: Report of Case with Involvement of Bronchi. E. B. Smith and L. M. Shefts, St. Louis.—p. 296.

Pulmonary Tuberculosis Complicated by Bronchial Tuberculosis.—Examination of complications arising in the course of administration of pneumothorax in pulmonary tuberculosis complicated by bronchial tuberculosis reveals, according to Rafferty and Shields, that atelectasis, anaerobic infection, progressive tuberculosis, tuberculous empyema and unexpandable lung occur frequently. These complications are so serious that every effort should be made to diagnose bronchial tuberculosis before pneumothorax is instituted for parenchymal disease. Prognosis in general depends more on the severity of the bronchial disease (and particularly its management) than on the stage of the pulmonary disease. Therefore the maintenance of an efficient bronchial drainage is of primary importance. Serious complications are encountered most often with extensive bronchial disease and especially when the inflammation is acute. Pneumothorax is contraindicated with extensive ulceration or stenosis and with moderate progressive or stationary ulceration, particularly if secretions are retained. It is relatively safe with moderate or slight ulceration which tends to heal. As the serious complications which follow pneumothorax often do not do so after thoracoplasty, it is therefore the treatment of choice when collapse therapy is indicated but pneumothorax is contraindicated.

Kentucky Medical Journal, Bowling Green

41:33-66 (Feb.) 1943

Fluorograph in Case Finding Program. T. A. Woodson, Louisville.—p. 35.
Planigraph in Pulmonary Lesions. E. R. Gernert, Louisville.—p. 35.
Acute Cholecystitis. F. M. Massie, Lexington.—p. 39.
Kenny Method of Treatment of Infantile Paralysis. R. T. Hudson, Louisville.—p. 44.
Kenny Treatment of Poliomyelitis. M. J. Wilder, Louisville.—p. 45.
Demonstration of Sister Kenny Treatment. J. J. Untereker, Louisville.—p. 47.
Muscular Dystropies or Myopathies. I. Kimbell, Lakeland.—p. 49.
Wartime Problems of Industrial Health. C. D. Selby, Detroit.—p. 53.
Military Roentgenology. R. E. Downing, Bowman Field.—p. 57.

Maine Medical Association Journal, Portland

34:25-44 (Feb.) 1943

State Responsibility for Tuberculosis Control. A. S. Pope, Boston.—p. 25.
Use of Outpatient Department in Control of Tuberculosis. D. Daniels, Greenwood Mountain.—p. 29.

Medicine, Baltimore

22:1-86 (Feb.) 1943

*Thymus in Relation to Myasthenia Gravis. D. McEachern, Montreal, Canada.—p. 1.
Present Status of Nonobstructive Jaundice Due to Infectious and Chemical Agents: Causative Agents, Pathogenesis, Inter-Relationships, Clinical Characteristics. R. Ottenberg and Rose Spiegel, New York.—p. 27.
Intravenous Alimentation with Amino Acids: G. J. Martin and M. R. Thompson, New York.—p. 73.

Thymus in Relation to Myasthenia Gravis.—McEachern states that the general character of myasthenia gravis suggests an endocrine disorder. Tumor or hyperplasia of the thymus is found at necropsy in more than half the cases. Microscopic search for aberrant or exceptionally small nodules might increase the percentage. The tumors are almost invariably benign encapsulated adenomas. Hyperthyroidism, adrenal cortex deficiency and castration each have muscular asthenia, creatinuria and hypertrophy of the thymus in common. The symptoms of myasthenia gravis are almost identical with those of prolonged curare poisoning, and the underlying neuromuscular disturbance is in both instances a peripheral phenomenon. The beneficial effects of prostigmine and the aggravation of symptoms by curariform drugs suggest faulty chemical transmission at the myoneural junction. Evidence favors the action of some curare-like substance. There is no convincing experimental evidence of an endocrine function for the thymus, although a number of observations are suggestive. Under clinical and experimental conditions the thymus undergoes hypertrophy during states of hyperthyroidism or hypofunction of the adrenal cortex or sex glands. Reverse conditions cause its involution. Since the thymus is largest at about the time of puberty and its weight in proportion to total body weight is greatest during the last months of fetal life and at birth, it might conceivably produce some substance which acts as a chemical brake to muscular activity, especially during fetal development. Roentgen evidence of thymic enlargement or tumor is rare in myasthenia gravis, although experience at necropsy leads to the anticipation of an abnormality of the organ in about half of the cases. Roentgen therapy directed to the thymus has yielded inconclusive results, although some patients seem to have benefited. Remissions and exacerbations of the disease in relation to pregnancy and to the alteration of the function of the thyroid are of great interest. The 13 patients with myasthenia gravis who had their thymus or thymic tumor removed and who survived appeared improved; the improvement in a few amounted to cure. Complete disappearance of myasthenic symptoms did not result in all cases despite apparently complete thymectomy. Experiments aimed to demonstrate a curare-like substance in the blood and urine of myasthenic patients and in extracts of thymic tumors removed at operation or necropsy revealed no such substance.

New England Journal of Medicine, Boston

228:113-144 (Jan. 28) 1943

Occurrence of Cor Pulmonale in Cases of Bronchial Asthma. I. W. Schiller, A. Colmes and D. Davis, Boston.—p. 113.
Dietary Study of Subjects from Upper Income Groups. H. T. Kelley and Myrtle Sheppard, Philadelphia.—p. 118.
Treatment of Common Skin Diseases. Beatrice Maher Kesten, New York.—p. 124.
Abdominal Surgery. A. W. Allen, Boston.—p. 127.

228:145-176 (Feb. 4) 1943

Pyogenic Liver Abscesses Due to Klebsiella Pneumoniae (Friedlaender's Bacillus). T. D. Kinney and H. S. Ginsberg, Boston.—p. 145.
Failure of Cobra Venom to Relieve Pain in Rheumatoid Arthritis. R. H. Talkov and W. Bauer, Boston.—p. 152.
Methyl Salicylate Poisoning: Report of 5 Cases. R. A. MacCready, Boston.—p. 155.
Hematology. W. Dameshek, Boston.—p. 157.

New Jersey Medical Society Journal, Trenton

40:41-80 (Feb.) 1943

Diagnosis and Treatment of Shock. R. H. Hill, Newark.—p. 51.
Syphilis in Relation to Iris and Uveal Tract: (Part of Symposium on Syphilis and Its Relation to Eye, Ear, Nose and Throat). G. P. Meyer, Philadelphia.—p. 55.
Development of and Responsibility for Local Health Work. R. C. Williams, New York.—p. 58.

North Carolina Medical Journal, Winston-Salem

4:41-76 (Feb.) 1943

Modern Concept of Hypertension. A. Grollman, Winston-Salem.—p. 41.
Roentgen Therapy in Treatment of Certain Inflammatory Conditions. R. J. Reeves, Durham.—p. 44.
Rorschach Test: Important Aid in the Personality Diagnosis. O. Billig, Asheville.—p. 46.
*Nicotinic Acid (Niacin) in Treatment of Vincent's Infection. W. M. Johnson, Winston-Salem.—p. 51.
Asheville-Buncombe County Gonorrheal Clinic for Women. Margery J. Lord, Asheville.—p. 51.
Significance of the Nasopharynx. M. B. Leath, High Point.—p. 53.
Cerebral Palsy and the Pediatrician. Grizzelle M. Norfleet and J. M. Arena, Durham.—p. 55.
History of Chinese Medicine. C. P. Bunch, Sturgills.—p. 58.

Niacin in Vincent's Infection.—Johnson gave 25 to 50 mg. of niacin three times a day to adults and 10 mg. or more to children with Vincent's angina. The most spectacular results were obtained in the acute cases. A typical case is that of a 17 year old girl with ulcers of the pharynx, enlarged cervical lymph nodes and a temperature of 103 F. A smear showed numerous Vincent's organisms. Niacin in 25 mg. doses three times daily resulted within forty-eight hours in normal temperature and disappearance of ulcers. A smear taken on the fifth day was negative. The substance was found useful in the acute cases of gum involvement and helpful in chronic cases in conjunction with local treatment. Its use keeps the mouth cleaner and apparently greatly retards the formation of tartar. It has been of decided value in pyorrhea even when Vincent's organisms were not present.

Northwest Medicine, Seattle

42:31-62 (Feb.) 1943

Gynecologic Aspects of Adolescence. G. C. Shauffler, Portland, Ore.—p. 35.
Physiology of Aging. A. J. Carlson, Chicago.—p. 46.
Surgical Management of Acute Cholecystitis. R. G. Andres, Spokane, Wash.—p. 48.
Neurologic Manifestations of Cardiovascular Disease of Sudden Onset. W. B. Dublin, Fort Steilacoom, Wash.—p. 52.

Ohio State Medical Journal, Columbus

39:97-200 (Feb.) 1943

Therapy of Pulmonary Irritant Gases. M. A. Blankenhorn, Cincinnati.—p. 113.
Cryptogenetic Pneumococcemia. J. M. Ruegsegger, Fort Bragg, N. C.—p. 117.
Blood Urea Nitrogen Elevation Associated with Sulfonamide Therapy. W. E. Molle and E. Woliver, Cincinnati.—p. 119.
Otitic Complications and Sulfonamides. H. G. Rubin, W. W. Sanger and J. B. McBean, Fort Sill, Okla.—p. 125.
Active Chemical Components of Crude Ragweed Extract. G. E. Rockwell, Cincinnati.—p. 128.
Calcific Aortic Stenosis. S. D. Simon, Cincinnati.—p. 133.
Treatment of Seborrheic Dermatitis. H. N. Cole, Cleveland.—p. 135.
Suggestions for Interns About to Become Medical Officers of the Army of the United States. W. L. Furste 2d, Camp Maxey, Texas.—p. 137.
McBurney Incision in Appendicitis: Cleveland Appendicitis Survey. J. D. Brett and R. M. Watkins, Cleveland.—p. 140.
Postpartum Myocardosis: Case Record Presenting Clinical Problems. R. W. Vilter and E. E. McKee, Cincinnati.—p. 142.
Importance of Zinc in Nutrition. J. Forman, Columbus.—p. 145.
Current Research in Allergy. J. H. Mitchell, Columbus.—p. 147.

Oklahoma State Medical Assn. Jour., Oklahoma City

36:47-92 (Feb.) 1943

Exigencies of Cardiovascular Origin. G. Herrmann, Galveston, Texas.—p. 47.
Tuberculous Tracheobronchitis. R. M. Burke, Oklahoma City.—p. 53.
The Irritable Bowel. T. Bynum, Chickasha.—p. 56.
Diagnosis and Treatment of Gallbladder Disease. D. D. Paulus, Oklahoma City.—p. 61.

Pennsylvania Medical Journal, Harrisburg

46:401-528 (Feb.) 1943

Survey of "Income Limits" for Subscribers to Nonprofit Medical Service Plans. R. W. Davies.—p. 447.
B Vitamins and Certain Problems They Present to the Practicing Physician. L. E. Holt Jr., Baltimore.—p. 451.
Adaptation of the Civilian Doctor to Army Practice. G. W. Wells, Fort Devens, Mass.—p. 459.
Psychoneuroses in Military Medicine. D. Whitehead, Fort Devens, Mass.—p. 463.
Question and Answer Period of Symposium on War Medicine. G. J. Kastlin, chairman.—p. 468.
Comparison of Different Complementary Feedings During First Two Weeks of Life. J. R. Noon Jr., Philadelphia.—p. 470.
Nutritional Condition of Philadelphia School Children. W. S. Cornell, Philadelphia.—p. 474.
Five Years of Pneumonia Control in Cambria County, Pa. B. J. McCloskey, Johnstown.—p. 478.

Psychosomatic Medicine, Baltimore

5:1-114 (Jan.) 1943

Psychosexuality in Schizophrenia: Some Endocrine Considerations. R. G. Hoskins, Boston.—p. 3.
Non-Neoplastic Hypergenitalism: Analysis of 17 Cases. N. Taylor and R. L. Schaefer.—p. 10.
Mental State Associated with Cerebral Lesions. L. B. Alford, St. Louis.—p. 15.
Evidences Concerning Neural Groundwork Underlying Certain Behavior Patterns. R. M. Brickner, A. A. Rosner and H. Yaskin, New York.—p. 20.
Dynamics of Selective Inhibition of Specific Functions in Neurosis: Preliminary Report. A. Wolf, Columbus, Ohio.—p. 27.
Bronchial Asthma in Functional Psychoses. H. C. Leavitt, Kankakee, Ill.—p. 39.
Psychiatric Observations in a Well Baby Clinic. Mabel Huschka and W. K. McKnight, New York.—p. 42.
Hypnotic Investigation of Psychosomatic Phenomena: I. Psychosomatic Interrelationships Studied by Experimental Hypnosis. M. H. Erickson, Eloise, Mich.—p. 51.
Id.: II. Development of Aphasia-like Reactions from Hypnotically Induced Amnesias: Experimental Observations and Detailed Case Report. M. H. Erickson, Eloise, Mich., and R. M. Brickner, New York.—p. 59.
Id.: III. Controlled Experimental Use of Hypnotic Regression in Therapy of Acquired Food Intolerance. M. H. Erickson, Eloise, Mich.—p. 67.

Public Health Reports, Washington, D. C.

58:297-336 (Feb. 19) 1943

Self Help Solution of State Personnel Problems. J. W. Mountin.—p. 297.
Toxicity and Histopathology of Some Azo Compounds as Influenced by Dietary Protein. M. I. Smith, R. D. Lillie and E. F. Stohlman.—p. 304.
Outbreak of Microsporon Lanosum Infection from Kitten. I. Botvinick, S. M. Peck and L. Schwartz.—p. 317.

58:337-376 (Feb. 26) 1943

*Practical Plan for Treatment of Superficial Fungous Infections. S. M. Peck and L. Schwartz.—p. 337.
Status of Full Time Local Health Organization at End of Fiscal Year 1941-1942. F. W. Kratz.—p. 345.
Experimental Rocky Mountain Spotted Fever: Results of Treatment with Certain Drugs. E. A. Steinhaus and R. R. Parker.—p. 351.
Triatoma Sanguisuga (LeConte) and Triatoma Ambigua Neiva as Natural Carriers of Trypanosoma Cruzi in Texas. D. J. Davis, T. McGregor and Thelma deShazo.—p. 353.

Treatment of Superficial Fungous Infections.—Peck and Schwartz differentiate fungous infections from the so-called allergic manifestations to them. The infected organism may become sensitized to the fungi or their products. Blood stream dissemination gives rise to manifestations known as dermatophytids. Secondary manifestations of dermatophytosis cannot be properly treated unless the primary infection is eradicated. Hypersensitivity to the fungi may be so great that only a small focus between the toes or under a toenail may result in generalized infections; that is, dermatophytids. In the treatment of direct dermatophytosis ointments should be used in the groin or other areas where there may be maceration. A typical formula for such an ointment approximates about half strength Whitfield's ointment with the addition of thymol. Tinctures may be found more practical. Trichophyton rubrum infections are extremely resistant to treatment. A conservative method for fungous infections of nails consists in daily scraping of the nail with a file or with sandpaper and the application of an antiseptic ointment or tincture. In some instances x-ray treatment has proved beneficial. Vleminckx's solution, boric acid

and Burow's solution in the form of wet dressings are helpful in deep dermatophytosis of hairy areas. Trichophyton metagraphyte, the most common cause of dermatophytosis of the feet, has a high sensitizing power. The most common form of dermatophytids associated with this fungous infection is manifested by vesicles along the sides of the toes. These have been called dyshidrotic epidermophytids. In addition to the local treatment, desensitization by injection of trichophytin must be attempted. The spread of fungous infections in shower rooms may be controlled by wearing individual slippers with wooden soles to and from and in the showers. These slippers can be sterilized once a week by placing them in 1 per cent saponated solution of cresol or by steam sterilization. In the acute stage of dermatophytosis of the feet with vesicles, swelling, erythema and pustules and a great deal of weeping, wet dressings are indicated. Foot baths with diluted saponated solution of cresol, about 0.5 per cent solution, taken two or three times a day for fifteen minutes are beneficial. Immersion in potassium permanganate 1:8,000, hot, for fifteen minutes two or three times a day is also helpful. Foot powder can be used between the baths. In the presence of a high degree of sensitivity and an eruption which has spread to the rest of the body it is not advisable to treat the primary lesion too vigorously because the rapid killing of fungi and dissemination of their toxins may cause intensification of the allergic manifestations. In the treatment of the subacute form a keratolytic and an antiseptic are needed. In some cases x-rays or trichophytin injections may have to be used. Infected socks should be boiled or treated by placing them in 1 per cent saponated solution of cresol, allowed to soak overnight and washed in cold water. Dusting powders may be used in the shoes. The infected socks and shoes may be placed in a closed receptacle and exposed to the vapors of formaldehyde.

Review of Gastroenterology, New York

10:1-76 (Jan.-Feb.) 1943

*Knott Technic of Ultraviolet Blood Irradiation as Control of Infection in Peritonitis. G. P. Miley, Philadelphia, and E. W. Rebbeck, Pittsburgh.—p. 1.
*Relation of Atrophic Gastric Mucosa to Carcinoma of Stomach. I. R. Jankelson, C. W. McClure, Boston, and H. Freedberg, Salem, Mass.—p. 26.
Benign Tumors of Stomach. G. S. Dudley, L. Miscall and S. F. Morse, New York.—p. 31.
Peptic Ulcer. G. McEvoy, Chestnut Hill, Mass.—p. 44.
Pruritus Ani: Tattoo Neurotomy. A. J. Cantor, Flushing, N. Y.—p. 46.
The Development of a Doctor. W. Walters, Rochester, Minn.—p. 49.
Gallbladder Problem. M. E. Rehfuss, Philadelphia.—p. 53.
Postsurgical Biliary Syndrome. J. W. Means, G. Y. Shinowara and C. J. DeLor, Columbus, Ohio.—p. 62.

Knott Technic of Ultraviolet Blood Irradiation in Peritonitis.—In the last four years Miley and Rebbeck irradiated the blood with ultraviolet to control the infection of 72 consecutive persons critically ill with peritonitis; 40 had generalized peritonitis, 20 appendical abscess with localized peritonitis and 12 multiple pelvic abscesses with severe pelvic peritonitis. In 43 the only therapy was the ultraviolet blood irradiation, and 29 were previously unsuccessfully treated with chemotherapy. The authors' technic of irradiating blood is that devised by Knott. The procedure consists in withdrawing and citrating a carefully predetermined amount of a patient's blood and immediately passing it through a hemoirradiator, a machine that properly irradiates the citrated blood and returns it intravenously to the patient. The end result of ultraviolet blood irradiation in the 40 patients with generalized peritonitis was that 32 recovered: 100 per cent of the moderately advanced and 53 per cent of the apparently moribund. Seventeen of the 20 with localized peritonitis with appendical abscess recovered: 100 per cent of the moderately advanced and 57 per cent of the apparently moribund. Nine of the 12 with pelvic peritonitis and multiple pelvic abscesses recovered: 100 per cent of the moderately advanced and 67 per cent of the apparently moribund. The paralytic ileus, which had been present as long as four days in some, disappeared within twelve to ninety-six hours after ultraviolet blood radiation therapy. This disappearance and the reappearance of normal intestinal smooth muscle tone was characterized by the expulsion of large amounts of flatus, a definite reduction in abdominal distention, normal abdominal auscultation and subsidence of other toxic symptoms. The optimal time for ultraviolet blood irradiation in all cases of peritonitis appears to be before operation, the sooner instituted the better.

Relation of Atrophic Gastric Mucosa to Gastric Carcinoma.—Jankelson and his associates found an incidence of 4 per cent of gastric cancer among 100 patients with pernicious anemia and an anticipated incidence of 4.4 per cent among 18 patients with atrophic gastritis. The actual or anticipated incidence of gastric cancer in the two groups was so high as to justify a conclusion that atrophy of the gastric mucosa predisposes to cancer. In the presence or absence of pernicious anemia, patients with atrophy of the gastric mucosa should be carefully observed lest an unsuspected gastric carcinoma develop. Repeated x-ray examination, gastroscopy and examination of the stool for occult blood should permit an early diagnosis of gastric polyps and carcinoma.

Tennessee State Medical Assn. Journal, Nashville

36:47-88 (Feb.) 1943

*Diagnosis and Treatment of Carcinoma of Colon. H. Wilson, Memphis.—p. 47.
Not All Men Think Alike. L. T. Buckman.—p. 57.
An Interpretation of Draft Rejection Figures. W. W. Bauer, Chicago.—p. 61.

Diagnosis and Treatment of Carcinoma of Colon.—The symptomatology of carcinoma of the right and left colon differs because of the anatomic and physiologic differences of the two sides of this organ. Wilson points out that mild digestive disturbances, changes in bowel habits, weakness and anemia should prompt an investigation of the right side of the colon. Chemical analysis is usually necessary to demonstrate blood from tumors of this side. Symptoms of acute, subacute or chronic obstruction are often the first evidences of a tumor of the left side of the colon. Progressive constipation occasionally replaced by an intermittent diarrhea is of common occurrence. Blood in the stool is apt to be present on gross examination. The diagnostic procedures in both instances should include history, digital examination of the rectum, stool analysis, proctoscopic examination and barium sulfate studies of the colon. A great deal of individualization of treatment is necessary in each case. The general physiology of the patient must be studied to ensure adequate levels of erythrocytes, plasma proteins, chlorides, water and protective vitamins. If obstruction exists it must be relieved by proximal decompression before the tumor is extirpated.

Virginia Medical Monthly, Richmond

70:67-120 (Feb.) 1943

Amebic Dysentery: Its Recognition and Treatment—Clinical Discussion. J. M. Ruffin, Durham, N. C.—p. 69.
Relationship of Hypertension to Surgical Diseases of Urinary Tract. A. I. Dodson, Richmond.—p. 72.
Our Duty as Physicians in Present Emergency—from a Patriotic Standpoint. W. C. Caudill, Pearisburg.—p. 78.
Care of the Mentally Ill in General Hospital. R. F. Gayle Jr., Richmond.—p. 80.
Roentgen Therapy of Brain and Spinal Cord Tumors in Children. F. B. Mandeville, Richmond.—p. 86.
Battle Casualties on the Home Front. P. Davis, Roanoke.—p. 90.
Subcortical Intracranial Hemorrhage of Surgical Significance: Report of Eight Cases. J. M. Meredith, Richmond.—p. 92.
Some Recent Advances in Diagnosis and Treatment of Cutaneous Fungous Infections. A. Pepple and R. W. Fowlkes, Richmond.—p. 101.
Eyes as Portal of Entry for Certain Air Borne Infections. K. D. Graves, Roanoke.—p. 104.
Treatment of Burns. M. K. King, Norfolk.—p. 106.
Keratitis Marginalis Superficialis—Acute Case. N. H. Turner, Richmond.—p. 109.

West Virginia Medical Journal, Charleston

39:69-104 (March) 1943

Proptosis as Diagnostic Problem. R. I. Lloyd, Brooklyn.—p. 69.
Spinal Anesthesia. E. M. Peck, Charleston.—p. 77.
Physiologic Approach to Water Balance of Surgical Patients. T. L. Harris and R. Jones Jr., Parkersburg.—p. 80.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

1:151-178 (Feb. 6) 1943

*Treatment of Cerebral Contusion. L. Rogers.—p. 151.
*Nature of the Rheumatic Child. D. Hubble.—p. 154.
Macrocytic Anemia of Pregnancy and Puerperium. H. W. Fullerton. —p. 158.
Economy in Fats and Oils in Treatment of Skin Diseases. G. H. Percival.—p. 160.
Bread Factor in Wartime Human Dietary. M. R. Richards.—p. 161.

Treatment of Cerebral Contusion.—Rogers presents evidence which indicates that the brain reacts to cerebral contusion by attempting to increase its volume. No two head injuries are exactly comparable. Remarkable and complete recoveries often follow extensive injuries to the skull and brain. The absence of sequelae following the consistent application of any particular therapy may be urged in its favor. Dehydration is a method which permits cerebral swelling to take place after injury. It should be effected by rectal administration of magnesium sulfate and not by intravenous methods, which probably cause undesirable reactions. A smooth convalescence and no sequelae have followed treatment of a large series of cases by continued gentle dehydration. Often the postconcussional state may result from the failure to introduce effective treatment in the early stages and it may represent a condition of unresolved contusion. It is believed that a resolution takes place readily and completely if the requisite condition for reparation is provided. This is the provision of space so that cerebral swelling can occur and is not restricted by the cerebrospinal envelops, with consequent impairment of the cerebral blood supply. Provision for such swelling is made by sustained dehydration, which reduces the incompressible water content of the skull.

The Rheumatic Child.—According to Hubble the rheumatic state in childhood has two main components—nervous excitability and infection. These are present in varying degree so that it may be impossible in one child to distinguish any nervous instability or in another to detect any evidence of infection. In one, the profound motor and emotional instability may be predominant and infection be either absent or a late invader, while in another infection dominates the picture at the onset and throughout its subsequent course. Growing pains usually result because of some difficulty attending the growth of the personality, not of stature, and it is easier to find evidence of nervous instability than of infection in the subacute rheumatic state. The nervous instability of the rheumatic child has no relation to neurosis; it is a quantitative increase in emotion and kinesis. The relationship between nervous excitability and infection is difficult to determine. It has been generally assumed that such nervous instability in a rheumatic child is the direct result of the "rheumatic infection or toxemia." This view is supported by the fact that chorea may develop for the first time during an attack of acute rheumatism. There is more evidence to support the contrary view that this nervous excitability commonly precedes infection and probably even prepares the ground for the rheumatic invader. The various etiologic factors in the rheumatic state are potent as far as they predispose to nervous excitability and infection. The heritable factor cannot be of great importance, as there are many facts that declare it primarily as an environmental disorder. The health of the rheumatic child is improved and stabilized by treating its nervous instability. This is done by the removal of the grosser environmental stresses, if possible, by the adjustment of the child's reaction to its environment and, most important, by continuous sedation with phenobarbital.

Edinburgh Medical Journal

50:65-128 (Feb.) 1943

Acute Aplastic Anemia Following Antisyphilitic Treatment. J. Grech, A. J. Rhodes and A. Grunberg.—p. 65.
Wound Hormones. J. N. Davidson.—p. 70.
Vitamins in Relation to Hemorrhage. H. Scarborough.—p. 85.

Journal Obst. & Gynaec. of Brit. Empire, Manchester

50:1-80 (Feb.) 1943

Study of Craniolacunia. J. B. Hartley and C. W. F. Burnett.—p. 1.
Maternal Birth Palsy Due to Trauma. H. H. F. Barns.—p. 13.
Lessons and Virtues of Salpingography: Improved Technic. V. B. Green-Armytage.—p. 23.
Simmonds's Disease Due to Postpartum Necrosis of Anterior Pituitary. H. L. Sheehan and N. G. B. McLetchie.—p. 27.
Accurate Pelvimetry. C. Nicholson.—p. 37.
Gangrene Occurring During Puerperium. G. B. Mair.—p. 44.
Observations on Shute's Test for Antiproteolytic Properties of Human Blood Serum in Cases of Abortion, Premature Labor, Accidental Hemorrhage and Normal Pregnancy. Vera I. Krieger.—p. 48.
Chorionepithelioma (Some Observations). H. E. Murray and H. Ahmed. —p. 55.
*Multiple Primary Cancers of Uterus. R. G. Maliphant.—p. 59.
Pregnancy and Labor Complicated by Ascending Myelitis and Bedsore of Unusual Size. J. B. Dawson.—p. 63.

Multiple Primary Cancers of Uterus.—The instance of multiple primary cancer of the uterus that Maliphant cites fulfilled the criteria for such a diagnosis: the cancers possessed distinct microscopic characters, different sites of involvement and complete independence. The entire corporeal endometrium of the author's patient was involved in a diffuse type of adenocarcinoma, while in the cervical canal there was an exophytic squamous cell carcinoma growing from its anterior wall. The demarcation of the tumors was clear, and any suggestion of transition from one to the other could not be detected.

Lancet, London

1:163-192 (Feb. 6) 1943

Diagnosis and the Patient. L. Cole.—p. 163.
*Orchiectomy in Cancer of Prostate. T. J. D. Lane.—p. 166.
Social Effects of Neurosis. A. Lewis.—p. 167.
*Erythropoiesis in Scurvy. M. C. G. Israels.—p. 170.
Bone and Joint Injuries. R. Watson-Jones.—p. 172.
Secondary Agranulocytic Angina. C. McGibbon and F. Glyn-Hughes. —p. 173.
Cannon Shell Injuries. R. Smith.—p. 175.

1: 193-224 (Feb. 13) 1943

Chronic Parkinsonism: Its Progress and Treatment. A. Hall.—p. 193.
Further Observations on Acute Staphylococcic Infection. E. C. B. Butler and F. C. O. Valentine.—p. 194.
Rehabilitation After Meniscectomy: Experience at an Army Convalescent Depot. J. J. R. Duthie and J. G. Macleod.—p. 197.
Chronic Melioidosis: Case Diagnosed in England. A. Grant and C. Barwell.—p. 199.
Hemolytic Anemia Due to Sulfapyridine. E. I. Jones.—p. 201.
Phosphorus Burns. E. Obermer.—p. 202.
Preparation of Grouping Serum. R. A. Shooter.—p. 202.
Group Psychotherapy for War Neuroses. D. Blair.—p. 204.

Orchiectomy in Cancer of Prostate.—Lane reports that, following orchiectomy, 23 patients with carcinoma of the prostate obtained almost immediate and complete relief from severe pain due to metastasis. His observations extend over six months. In many instances the consistency and mobility of the prostate were apparently restored to normal or much improved. The general health was commonly benefited. Estimations of the blood acid phosphatase ranged from 23 to 77.5 units per hundred cubic centimeters in cases in which there was x-ray evidence of bone metastasis. In all cases there was urinary retention, which was relieved by a Thompson punch resection. Postorchiectomy estimation of the blood phosphatase is likely to prove useful in the management of these cases. Huggins and his colleagues suggest that if the acid phosphatase of the serum does not reach a low level after castration androgens are presumably being produced outside the testis; this is an indication for estrogen therapy.

Erythropoiesis in Scurvy.—Israels describes the changes in the bone marrow in 3 cases of scurvy and anemia before and after treatment with ascorbic acid. In 2 there was evidence of diminished erythropoiesis, and in 1 erythropoiesis was not significantly abnormal. After treatment with ascorbic acid erythropoiesis of the bone marrow was increased in all cases. The anemia also improved rapidly without any specific antianemic treatment. Ascorbic acid deficiency seems to be more a depression of erythropoiesis than a failure of maturation. The present shortage of ascorbic acid in the diet may eventually lead

to depression of erythropoiesis, and consequent anemia should be borne in mind, especially under present conditions of dietary restriction. The increased incidence of anemia, particularly among pregnant women, because of an inadequacy of iron in the diet has been suggested as the cause. Also a diet deficient in ascorbic acid may well be a contributory cause of this anemia. Ascorbic acid should be given to any patient whose anemia does not respond satisfactorily to iron.

Gastroenterologia, Basel

66:249-360 (Nos. 5 and 6) 1942

Intramural Course of Blood Vessels of Small Intestine: Functional Structure of Intestinal Wall. G. Wolf-Heidegger.—p. 249.
Sphere of Activity of Hemopoietic Substance in Pernicious Anemia. C. D. de Langen.—p. 288.
Gastroscopic Studies Following Abdominal Operations: Late Gastroscopic Picture After Perforation of Gastroduodenal Ulcers. L. von Friedrich.—p. 298.
*Treatment of Ulcerative Colitis by Salicylazosulfapyridine. Nanna Svartz.—p. 312.
*Clinical Observation on Lambliasis. P. R. Dreyfus.—p. 323.
Therapy of Peptic Ulcers with Sex Hormones. C. Adams.—p. 343.

Salicylazosulfapyridine in Ulcerative Colitis.—Svartz experimented with a new sulfonamide compound, salicylazosulfapyridine, which had been found effective in polyarthritis. She reports the effects of salicylazosulfapyridine in 5 cases of ulcerative colitis. Salicylazosulfapyridine appears to be the best available medicament against ulcerative colitis. Two tablets of 0.5 Gm. each were given from four to six times daily. After the symptoms of ulcerative colitis subsided the treatment was continued in gradually decreasing doses for approximately a month. Administration of the drug is fairly frequently accompanied by fever and rashes, while other complications are rare. Investigations revealed that the sulfapyridine constituent is the cause of skin eruptions. Skin tests are of no value in the detection of hypersensitivity to either salicylazosulfapyridine or sulfapyridine; patients who have given negative cutaneous reactions exhibited signs of hypersensitivity. Aminopyridine, a substance which probably forms in the organism as the result of the cleavage of sulfapyridine, gives a positive cutaneous reaction in patients who have had an exanthem after medication with salicylazosulfapyridine.

Clinical Observation on Lambliasis.—Dreyfus reviews the symptomatology of lambliasis on the basis of 16 cases observed at the medical clinic of Lausanne. The condition was formerly regarded as rare and harmless. The use of the duodenal tube has demonstrated that it is comparatively frequent. The effects of lambliasis are not limited to the intestine and the biliary system; the toxins of lamblia organisms may act on the nervous system, the hepatic parenchyma and the reticuloendothelial system and may cause grave changes in the general condition. In the presence of clinical pictures with obscure etiology, lamblia should be systematically searched for. Acridine dye preparations, such as atabrine or acranil, permit a "therapia sterilisans magna."

Schweizerische medizinische Wochenschrift, Basel

72:1025-1052 (Sept. 19) 1942. **Partial Index**

Epidemiology of Poliomyelitis. G. Fanconi and H. Zellweger.—p. 1025.
Dietetic Therapy in Rheumatic Diseases and Its Use in Military Hospitals. O. Gsell.—p. 1029.
Sulfonamide Therapy in Acute Streptococcic Nephritis and Typhoid and Paratyphoid. M. P. Marcel.—p. 1032.
Combined Cranial, Cerebral and Ventricular Volumetry. R. de Montmollin.—p. 1038.
*Hepatogenic Osteodystrophies. G. Mayor.—p. 1042.

Hepatogenic Osteodystrophies.—Leriche and Jung called attention to the faulty union of fractures in subjects with hepatic lesions, particularly with biliary fistulas. Systematic study of hepatic disorders, such as cirrhoses and hepatic or biliary cancer, and of severe hepatic disorders secondary to acute yellow atrophy or to a hemorrhagic cholangitis demonstrated that these disorders are constantly accompanied by osseous lesions. Mayor confirmed these observations in experiments on rats and dogs. The polymorphism of bony alterations in persons with grave hepatic disorders does not permit the conclusion that the skeletal defects are secondary to loss of bile. Serologic analyses demonstrate that disease of the liver brings about a complex disturbance of the metabolism, of a number of elements essential to the development of the organism. Taken individually, these manifestations do not explain the bony disturbances; their combination, however, seems sufficient to explain those which the author classifies as hepatogenous osteodystrophies. Disturbance in the fat metabolism in the case of insufficient biliary excretion is at the base of poor calcium assimilation, the fats being eliminated by the intestine in the form of calcareous soaps. A pathologic fat excretion leads to a loss of calcium. Biliary salts play the role of a co-ferment with regard to the pancreatic lipase and increase the hydrolytic power of the pancreatic juice toward neutral fats. Bile contains substances indispensable to the breaking down of soaps and fatty acids. Insufficiency of biliary excretion leads to faulty fat absorption. Steatorrhea and faulty calcium absorption which it involves have been known for a long time. The author discusses disturbances in the vitamin D and A metabolisms and the involvement of the parathyroids, and the hypophysis in hepatic disorders. Hepatogenic bone lesions should be classified with the endogenous types of osteodystrophies of visceral character similar to the renal and pancreatic osteodystrophies.

Archivos Argentinos De Pediatría, Buenos Aires

18:327-420 (Oct.) 1942

Hemorrhagic Pachymeningitis. R. P. Beranger and L. M. Codeglia.—p. 327.
Acute Aseptic Puriform Meningitis. R. Cibils Aguirre, Sara de Alzaga and D. Aguilar Giraldes.—p. 333.
*Cerebral Hemorrhages in the Newborn. E. Halac and J. J. Halac.—p. 342.
Normal Values of Alkali Reserve in Nurslings. M. J. del Carril, A. E. Larguia, M. Gori and J. C. Vidal.—p. 360.
Sudden Death in Early Infancy. J. M. Albores.—p. 365.

Cerebral Hemorrhages in the Newborn.—The Halacs collected cases of cerebral hemorrhage in the newborn in the institute of maternity in Córdoba during the last four years from a total number of 5,812 deliveries. They found that children of primiparas die of cerebral hemorrhage more often than do those of multiparas, the percentages being 1.27 and 0.85 respectively. Abnormal presentations and obstetric manipulations are likely to cause cerebral hemorrhage. The authors observed the following mortality rates in the different presentations: vertex 0.59 per cent, brow 33⅓ per cent, face 7.4 per cent, pelvic 6.6 per cent. This suggests that an abnormal presentation is to be converted into a less dangerous one. Narrow pelvis and other obstacles to delivery involve dangers for the fetus if they are not discovered until after delivery has begun. Efforts should therefore be made to diagnose them early. Dystocia caused by abnormal uterine dynamics may have a traumatizing effect on the fetus. Use of substances capable of counteracting these dystocias will remove factors likely to elicit cerebral hemorrhage in the fetus. Correct selection of the obstetric intervention and the careful execution are of great importance; cerebral hemorrhages were present in 5.86 per cent of the children delivered with forceps, in 11.22 per cent of those delivered by internal rotation and extraction and in 7.68 per cent of those delivered by cesarean section. Syphilis and toxemia of pregnancy may cause changes in the tissues of the fetus. Their early detection and treatment will reduce the percentage of infants with cerebral hemorrhage. Women with menstrual disturbances have a high rate of artificial deliveries of infants who die of cerebral hemorrhage. If a child is born with any of the aforementioned antecedents and manifests asphyxia, resuscitation measures should be carried out cautiously and cerebral hemorrhage should be thought of. Immediate and prolonged immobilization (fifteen to twenty days) is indicated. Ice should be applied to the head; vitamins C and K and coagulating substances should be administered. At the author's clinic in Córdoba vitamin K is injected routinely into all parturient women in whom prolonged labor or obstetric manipulations seem likely.

Book Notices

Fractures of the Jaws and Other Facial Bones. By Glenn Major, D.D.S., M.D., F.A.C.S. With Chapters on Radiographic Technic, by Lester M. J. Freedman, B.S., M.D., Acting Director, Department of Radiation Therapy, the Western Pennsylvania Hospital, Pittsburgh, and War Aspects of Jaw Fractures, by Arthur Dick, D.D.S., M.D., Major, Medical Corps, Army of the United States. Cloth. Price, $7.50. Pp. 446, with 225 illustrations. St. Louis: C. V. Mosby Company, 1943.

This textbook is of interest and value to the physician, the surgeon and the dental surgeon. This is particularly true now that large numbers of civilian doctors are joining military and naval services. They must be acquainted with the pathology and basic surgical principles involved in the management of these fractures. The text is easily readable by the general practitioner. It presents the essential basic facts pertinent to the subject which make it valuable to the surgeon and to the dentist who has not enjoyed a special training in oral surgery.

Chapters on diagnosis, the mechanics of displacement of the fragments, emergency collateral treatment and the general principles of the reduction and fixation of fractured segments cover the subjects adequately and simply. The various types of reduction and fixation generally employed in fractures of the mandible and maxilla are clearly and adequately described and well illustrated with drawings by the author. These principles and methods are applied to "special fractures" in the following chapters. These present the fundamentals essential to the management of the variously located sites of fracture and the numerous combinations of circumstances presented in both dentulous and edentulous jaws. Fractures of the malar compound are discussed similarly. The management of nasal fractures is discussed too generally and too briefly. This type of fracture is not well handled in civilian practice as a rule and this occasions much subsequent surgery which could be avoided. The mechanical devices described are rarely essential to a good result. Postoperative care, diet and complications are sufficiently discussed. Chapters on radiographic technic and the war aspects of fracture casualties will be helpful to the military surgeon.

A good index and generous subheadings throughout the text make the subject matter readily accessible. The volume should be in the hands of every practitioner.

Speaking of Man: A Biologist Looks at Man. By Michael F. Guyer, Professor of Zoology, University of Wisconsin, Madison. Cloth. Price, $3.50. Pp. 321. New York & London: Harper & Brothers, 1942.

This book is a rather uneven combination of scientific facts for the layman, biologic interpretations of human behavior, common sense observations about everything, and poetry. Professor Guyer is at his best in his exposition of the value of science and in his lucid and interesting presentation of the findings of astronomy, chemistry, biology and psychology. The book would have gained in consistency and power if it had been confined to the definition of scientific method and to a summary of scientific knowledge. The biologic interpretations of behavior are inadequate and onesided, since the author does not integrate them with the points of view of social psychology and anthropology, of which he shows little or no knowledge. His observations on human conduct are wise and witty but are often unrelated to his scientific facts and biologic point of view. They seem frequently to arise more out of his experiences as a person in our American culture than out of his experiments in the laboratory. This is almost inevitable when a specialist attempts to apply his knowledge gained in one small field to the whole area of human behavior, including sex, education, democracy and international relations. Many readers will be uplifted by the quoted poetry and Professor Guyer's own prose poetry.

Obstrucción del colédoco y decompresión del sistema biliar obstruído: Estudio de cirugía experimental, consideraciones clínico-quirúrgicas. Por el Dr. Abel N. Canónico. Tesis de doctorado, Universidad nacional de Buenos Aires, Facultad de ciencias médicas, Escuela de medicina. Paper. Pp. 149, with 66 illustrations. Buenos Aires, 1938.

A good experimental study of the lesions induced by bile duct obstruction. The black and white and colored illustrations are as good as those seen in first class textbooks, if not better. Since comprehensive summaries in English, French and German are appended and the publication is available for exchange, we can dispense with an analysis of the author's conclusions.

Clinical Laboratory Diagnosis. By Samuel A. Levinson, M.S., M.D., Director of Laboratories and Pathologist, Research and Educational Hospitals, Chicago, and Robert P. MacFate, Ch.E., M.S., Ph.D., Assistant Director of Laboratories, Research and Educational Hospitals. Second edition. Cloth. Price, $10. Pp. 980, with 171 illustrations. Philadelphia: Lea & Febiger, 1943.

The second edition of this excellent book has been thoroughly revised and brought up to date. New methods have been added where experience has shown them to be of value. Old methods which have proved of little worth in the light of recent investigations have been deleted. The latest interpretations of clinical laboratory findings and many new items have been included. There are sufficient illustrations, including several colored plates of skin reactions. The first edition proved its general usefulness. As a textbook for students in clinical pathology it served as a guide for general laboratory technic and as the basis for well recognized interpretations of laboratory findings. Detailed discussions were limited to matters not previously covered in the general medical curriculum. Reference was made to a few pertinent items from previous studies to serve as a reminder of all the work that had gone before. Most of the controversial points were reserved for the lecture room. The intern and the practicing physician have found the book of value in the interpretation of laboratory findings and as an aid in the study of cases requiring laboratory work. In the clinical laboratories of the average hospital it serves as a quick ready aid. The method of presenting the various laboratory technics in simple and concise terms has served to meet the needs of the laboratory technician, from the inexperienced beginner to the highly trained medical technologist and clinical pathologist.

Additions to the second edition include discussions of water metabolism, acid-base balance, bone marrow findings, blood volume, the Rh factor, prothrombin and many other items which have become more important in the past few years. The chapter on blood chemical methods has been brought up to date and methods for the photometer have been added. This section should prove of great value to the clinical laboratory, because methods have been modified so that the same reagents are used whether the product is to be read in the colorimeter or in the photometer. At all times, but especially in the present emergency, clinical laboratories are faced with the problem of performing tests when the apparatus used needs repair. The colorimetric determinations here presented may be converted from the photometer to the colorimeter or the reverse with but slight changes in technic and with no loss of time for the preparation of new reagents. Thus, continuation of the normal routine may be effected when either the photometer or the colorimeter requires repair. Among the new blood chemical methods described are ascorbic acid, acid and alkaline phosphatase, amylase, bromine and sulfonamide compounds. The comprehensive tables of normal and abnormal findings have been revised. The latest approved changes in the Kolmer complement fixation test, the Kahn test and other serodiagnostic tests have been added. The chapter on general bacteriology has been completely revised with the addition of detailed technic for the initial isolation and final identification of all the common bacteria. The comprehensive tables of the characteristics of the more common bacteria have been revised. Two excellent color plates of bacteria have been added. Bergey's latest nomenclature and classification have been followed thoroughout. Extensive revisions have also been made in the chapters on sputum, pediatric procedures, histologic technic and legal medicine.

The systematic arrangement of the book follows that of the first edition. Extensive use has been made of charts and tables, which are especially valuable. The outline of the course in clinical pathology which appeared in the first edition has been deleted to allow more room for recent important tests. Aside from this deletion, more than a hundred and sixty pages of text have been added. The book is unique in its comprehensiveness without any sacrifice in clarity of subject matter. Its usefulness has been proved and it has been accepted as a standard work on clinical laboratory diagnosis. The book is unqualifiably recommended to technicians, students, clinical pathologists and physicians.

The Sight Saver. By C. J. Gerling. Cloth. Price, $2. Pp. 202. New York: Harvest House, 1943.

The author is not a physician and is known to the reviewer as author of this book and another, "The Complete Weight Reducer." This book is written to acquaint laymen with the essential facts about the eyes and to warn them against the methods employed by quacks. It seems admirably conceived for this purpose. The facts about the eye and its functions are given in concise paragraphs, arranged alphabetically, with cross references to other related sections. It is debatable whether this arrangement is conducive to pleasant reading, but it does allow a reader to find easily the information available on any subject. The information was obtained from a number of books and pamphlets both medical and popular, which are listed and seem to have been well selected. Being written by a layman, the language is such as to be easily understood by laymen.

The author represents consistently the views held by most ophthalmologists. One might point to instances of undue optimism concerning the effects of treatment in certain diseases and to an unduly pessimistic attitude toward the result of surgery in strabismus. On the whole, however, the information is such as any ophthalmologist would be glad to place in the hands of his patients.

At this time, when popular enthusiasm has been fanned by Huxley's book on the Bates method of correcting eye defects by exercise, it is worth quoting part of what the author has to say about Dr. Bates and his methods: "Though a graduate of a recognized medical school, Bates enjoys the dubious honor of being the patron saint of the multitude of charlatans who prey upon persons whose vanity or convenience brought them to seek to escape the need for wearing glasses." Under "Quackery and Fraud" the author goes further into this matter and into other forms of deception which have such a strong appeal to those with ocular ailments. Various well advertised eye drops are described with advice that boric acid solution or isotonic solution of sodium chloride is as good when a cleansing solution is required. Patients are cautioned against self medication and against a number of beauty aids for use about the eyes.

The functions of the eye physician, optometrist and optician are well defined, and the advantages of examination by the physician are stressed. The section on the price of glasses is a fair discussion of this touchy subject.

The Mind and Its Disorders. By James N. Brawner, M.D., Medical Superintendent, Brawner's Sanitarium, Smyrna, Georgia. Cloth. Price, $3.50. Pp. 228, with 7 illustrations. Atlanta: Walter W. Brown Publishing Company, 1942.

The author, superintendent of a sanatorium, purports to describe briefly and in simple language the neuroses, psychoneuroses and psychoses, writing especially for the general practitioner. Part I is a brief account of the mind as related to cerebral structures and functions. Included here are such subjects as feelings and emotions, intelligence, memory, excitation and inhibition, and the electroencephalogram. No attempt is made to give an adequate account of these fundamental subjects, and the psychologic approach is essentially that of the old "faculty" school. The diagrams illustrating cerebral structures are poorly labeled and give a confused impression of brain centers and their function. Part II is an account of the etiology, symptoms and treatment of the psychoses. Here the psychoses are defined as "disordered intellectual or emotional reactions due to defective heredity, acquired diseases, environmental experiences" or their combinations. Obviously this definition makes no distinction between defects, such as simple schizophrenia, dementia, which may occur without psychosis, psychoneuroses, in which the stress is between the patient and his environment, and the psychoses, in which the stress is primarily within the body. This section of the book is quite complete topically, and the author is to be commended for stressing the view that the subject matter of psychiatry is closely related to internal medicine. The modern shock treatments are described and recommended. Part III is a description of the neuroses and psychoneuroses, the former being regarded as an "abnormal nervous reaction, involving principally the vegetative and lower cerebrospinal mechanisms, while the psychoneuroses involve to a limited extent the mental processes." Suggested treatment is essentially that of diet, hydrotherapy and recreation. Little attention is given to the need for analysis of the highly important psychologic factors in many of these disturbances. Part IV includes a number of related subjects. The book gives a rapid review of mental disorders, and, despite shortcomings which limit its interest to the trained psychiatrist, it should prove of value to the general practitioner as an aid to his understanding of mental disorders.

Pancreatic Function and Pancreatic Disease Studied by Means of Secretin. By Henrik O. Lagerlöf, M.D. Translated by Helen D. Frey. With a foreword by Joseph H. Pratt, M.D. Cloth. Price, $3.50. Pp. 289, with 10 illustrations. New York: Macmillan Company, 1942.

In his foreword to this monograph, Dr. Pratt summarizes its import by saying that the work reported by Lagerlöf has lifted pancreatic analysis to the level gastric analysis has occupied for many years. Almost half of the volume is concerned with a historical survey of research on the physiology of the pancreas and a description and critique of methods for the analysis of the pancreatic enzymes. There follows a relatively brief section on the secretin test as used by the author and his collaborators, and the results obtained with it on normal individuals and on patients suffering from pancreatic disease. The remaining approximately one third of the book is devoted to summarized case histories of 37 patients with proved diseases of the pancreas and of 26 patients with suspected pancreatic disease. An appendix contains tabular data illustrating the author's experimental work and summarizing control tests on normal subjects. A bibliography of 358 references is also included. This book is a useful reference work for physiologists and for students of gastroenterology. The practical considerations of immediate interest and use to the general practitioner might well have been set forth in a pamphlet only a fraction of its size.

Noxious Gases and the Principles of Respiration Influencing Their Action. By Yandell Henderson and Howard W. Haggard. American Chemical Society Monograph Series. Second edition. Cloth. Price, $3.50. Pp. 294, with 12 illustrations. New York: Reinhold Publishing Corporation, 1943.

This book is another in the American Chemical Society's Series of Scientific and Technologic Monographs. According to the authors it is written for the practical use and information of chemists, engineers and others engaged in industry. As far as the medical profession is concerned, the book will be of value to industrial physicians and lecturers on industrial medicine. It does not seem suitable for students except as a reference source. Included in the contents are chapters covering a general survey of the field, elements of respiration, the respiratory functions of the blood and their laws and practical applications of the laws of gases and vapors. Of special interest are the chapters offering discussions on the principles determining absorption, distribution and elimination of volatile substances and classification and descriptions of noxious gases and vapors. Supplementing this information are practical statements on methods of resuscitation, first aid and prevention of poisoning by noxious gases.

Técnica e indicaciones de la transfusión en el niño pequeño. Por Gualterio Federico Thomas. Tesis, Universidad nacional de Buenos Aires, Facultad de ciencias médicas, Escuela de medicina. Paper. Pp. 68, with 20 illustrations. Buenos Aires, 1942.

In this study the author advises the use of peripheral veins for blood transfusions in little children and infants and gives useful data concerning the indications of the method.

Big Little Things in Conquering Pulmonary Tuberculosis. By Samuel H. Watson, M.D., and W. R. Hewitt, M.D. Second edition. Paper. Price, 10 cents. Pp. 28. Tucson, Ariz.: Tucson Clinic, 1943.

This pamphlet is devised for patients with pulmonary tuberculosis who must become adjusted to an entirely new routine of life. It answers the common questions of patients in a straightforward and common sense manner. It can be safely recommended to all patients who have learned of their tuberculosis for the first time.

El nistagmus postoperatorio en neurocirugia. Por el Dr. Fermin J. Barcala. Tesis de doctorado, Universidad nacional de Buenos Aires, Facultad de ciencias médicas. Paper. Pp. 68. Buenos Aires: Aniceto Lopez, 1942.

A study of nystagmus developing after craniectomy, of which the etiology is unknown but the disappearance of which seems to parallel the disappearance of cerebral edema.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

TESTING AND RECORDING VISUAL ACUITY

To the Editor:—**What is considered "standard" in testing distant and near vision: Is 20 feet "standard" for distant vision? Is 14 inches "standard" for near vision? If a photometer when placed in the same position as the examinee's eyes reads 25 foot candles is that considered "standard"? If you are unable to answer this in terms of "standard," how would you answer it in terms of recommendations?** M.D., New Jersey.

ANSWER.—It is impossible to apply the term "standard" to the testing and recording of visual acuity. It is not the distance between the patient and the test chart that is the deciding factor, but the angle that letters of a given size produce on the retina. Snellen, who introduced the present method of recording, utilized 20 feet because that was the most feasible under his working conditions. Ophthalmologists refract at 20, 30 or 40 feet or at 6 or 10 meters according to the available space. Test charts are graded accordingly and the results are recorded by a ratio, of which the working distance is the numerator. Thus 20/20 corresponds to 30/30, 40/40, 6/6 or 10/10. Thus the available working distance is the determining factor, and, when that has been decided on, test charts should vary so that the angular size of the letters corresponds or the ratio of the charts used should be transposed.

Fourteen inches was adopted as the average reading distance by the Committee on Compensation for Visual Injury, and the near chart was so constructed that the letters on that chart subtended an angle of 5 minutes on the retina. The reader is referred to the report of this committee, which appeared in THE JOURNAL, July 11, 1925, page 113.

The photometer reading should be at the test chart and not at the patient's eye. At that point the intensity of illumination must be not less than 10 foot candles nor more than 25.

PAINFUL RECURRENT ULCERS OF MOUTH

To the Editor:—**A white woman aged 60 complains of recurrent ulcers of the mouth, first beginning with the menopause. They are flat, irregular, shallow ulcers with a purulent base and are associated with excruciating pain, recurring from two to four times a year. They are slow to heal. She has been thoroughly studied by a number of competent physicians with no significant positive findings. Her general condition is excellent. Do similar conditions occur as a result of endocrine dysfunction? Kindly suggest methods of treatment or prevention.** M.D., District of Columbia.

ANSWER.—The ulcerative stomatitis which has been briefly described fits with the diagnosis of periadenitis mucosa necrotica recurrens. This is a familial condition said to be endocrine in origin, occurring in older women. The description of the ulcers with pain is typical, and their tendency to recur is noted in the name. None of the treatments proposed have proved consistently successful.

Local treatment with alum, and the use of solution of potassium arsenite internally, have been recommended. A trial of ovarian substance (theelin) by injection or orally would be worth while.

Simple ulcerative stomatitis in general is rare in good health and may suggest an early dietary deficiency, especially if the oral hygiene and condition of the teeth are good.

Potassium chlorate 0.65 Gm. three times a day is said to be effective.

Fusospirochetal ulcers may be recurrent and may offer little in the way of definite bacterial flora except on repeated examination. The use of neoarsphenamine in glycerin (10 per cent) alternating with sodium perborate packs would be worth a trial if this condition seems probable.

TREATMENT OF INTERNAL HEMORRHOIDS

To the Editor:—**Will you please inform me as to the status of electrocoagulation in the treatment of internal hemorrhoids? Is it an accepted procedure?** Louis B. Sternberg, M.D., Shelbyville, Ky.

ANSWER.—As far as is known, electrocoagulation is not used extensively in the treatment of internal hemorrhoids. Doctors who treat internal hemorrhoids are more likely to use an injection of carbolic acid solution or quinine and urea hydrochloride. The technic for these injections and the strength of the solution can be found in any textbook of surgery. Either of the methods, electrocoagulation or injection of irritating solutions, causes thromboses in the veins of the internal hemorrhoids which later result in fibrosis and some shrinking of the hemorrhoids. The difficulty with the whole procedure is that any other lesion such as polyps, fissures or external hemorrhoids covered by skin are not amenable to treatment. Therefore only a limited number of patients should be treated in this manner and those with careful selection. If these precautions are neglected, patients frequently are made worse by injections or electrocoagulation and suffer from ulceration, hemorrhage or abscess formation. In addition, most dilated veins causing hemorrhoids are present under the skin as well as under the mucosa, and the veins under both areas anastomose freely with one another. If only one group is treated, leaving the other, recurrence is almost inevitable. This means that the treatment of internal hemorrhoids by electrocoagulation or injection treatment is probably but a palliative measure in most instances.

GONOCOCCI AND OTHER ORGANISMS GIVING POSITIVE OXIDASE REACTION

To the Editor:—**With regard to culturing gonococci on chocolate blood agar medium, I should appreciate information on organisms other than gonococci that give oxidase reactions that would be likely to be normal inhabitants of the vaginal tract. Also may I have information concerning the gram staining properties as well as the general morphology of these organisms if any? I am also interested as to the sugar fermentation reactions of any organisms that might be confused with gonococci when using the oxidase method of detection of gonococcus colonies by culture method.** Albert R. Cameron, M.D., Wilmington, N. C.

ANSWER.—When J. W. McLeod (*J. Path. & Bact.* **31**:185, 1928) introduced the use of the oxidase test for rapid identification of the gonococcus, he gave a list of other organisms which were oxidase positive. Those which have been encountered occasionally in the genitourinary tract are other Neisseria (catarrhalis, flava and sicca), Hemophilus, certain yeasts, some varieties of the coliform bacillus and Bacillus subtilis and Streptothrix which occasionally occur as contaminants. Organisms which have not been completely identified have also been reported: McLeod (*ibid.* **39**:221 [July] 1934) and Price (*Brit. M. J.* **1**:199 [Feb. 2] 1929) small gram-negative diplococci, Luther Thompson (*J. Bact.* **31**:82 [Jan.] 1936) a gram-negative diplobacillus, Weiss and Calvin (*South. M. J.* **34**:1102 [Nov.] 1941) a gram-positive bacillus.

Less than 2 per cent of the positive reactions are due to these organisms and many of them can be differentiated on the basis of morphology alone. The others can be ruled out by fermentation reactions.

McLeod (*J. Path. & Bact.* **39**:221 [July] 1934) and certain other workers, Thompson (*J. Infect. Dis.* **61**:129 [Sept.-Oct.] 1937), Spohr and Landy (*J. Lab. & Clin. Med.* **21**:650 [March] 1936), Hac, Hesseltine, Adair and Hibbs (*Am. J. Obst. & Gynec.* **41**:98 [Jan.] 1941) have found the tetramethyl p-phenylene diamine hydrochloride preferable to the dimethyl compound for differentiation.

It must also be remembered that an occasional strain of gonococcus will fail to give a positive reaction to the oxidase test, at least on primary isolation (Pitts, A. C.: *Am. J. Syph., Gonor. & Ven. Dis.* **24**:184 [March] 1940).

Additional references:

Leahy, A. D., and Carpenter, C. M.: *Am. J. Syph., Gonor. & Ven. Dis.* **20**: 347 (July, pt. 1) 1936.
Sulkin, S. E., and Gottlieb, Eleonore, *ibid.* **25**: 22 (Jan.) 1941.
Jacobsen, Frances; Mason, H. C., and Arnold, Lloyd: *J. Lab. & Clin. Med.* **23**: 729 (April) 1938.

SNAKEBITE AND INTELLIGENCE

To the Editor:—**The bushmaster snake with neurotoxic venom is found in the jungles of eastern Peru. At a mission on the Perene River I saw a normal Indian who had recovered from the bite and who was said to be more intelligent than previously. This is the usual result. How does this compare with the use of snake venom in the treatment of insanity?** Roland Young, M.D., Casapalca, Peru.

ANSWER.—Record has not been found in the scientific medical literature concerning the treatment of insanity with snake venom. One snake dealer has been treated for five different bites and his wife for seven bites. Since they continue to handle snakes after being bitten five and seven times respectively, this seems to offer conclusive proof that this venom has not given them any excess of intelligence. There is no evidence that the snake handlers in carnivals appear to possess superior mentality, and horses which are used to make antiserum do not form an especially happy looking lot.

PELVIC MASS AND ABDOMINAL FISTULAS

To the Editor:—A woman aged 27 was taken acutely ill about five months ago and had to be hospitalized at that time. A right lower quadrant incision was made and a pelvic mass found. Small intestinal loops which adhered to the mass were peeled off and the mass was drained. About three weeks after the first operation an incision on the left side was made for drainage of the mass. About three months after the first operation the pelvic mass was removed. A biopsy after the second operation indicated some kind of fungous disease. A culture of the pus taken out of the mass at the time of the third operation yielded Leptothrix. About one month after the third operation a foreign body 2.5 cm. long at one end and 3 mm. wide tapering to a point at the other end was expelled through a fistula. At present the patient is anemic. There are three fistula openings on the abdomen. There is a small mass in the left lower quadrant that causes pain. The general condition is poor. What should be done for the Leptothrix infection? Do you think that the expulsion of the foreign body, which seemed to be wood, on Jan. 16, 1943 may still result in healing without further medication or intervention?

Alexander Strelinger, M.D., Elizabeth, N. J.

ANSWER.—Because of the poor condition of the patient, all aids must be employed to build up her resistance by prescribing a properly balanced diet and extra vitamin B complex and perhaps also by giving one or more blood transfusions. Roentgenograms, both anteroposterior and lateral, should be taken and a search made for additional foreign bodies. If none are found the treatment should be conservative, because it is possible that after a while the fistulas may close spontaneously. If a foreign body is found an operation will most likely be necessary, but this should not be performed until the patient's condition is considerably improved. This may require many months. In some instances a foreign body becomes walled off by adhesions and no harm results from leaving it. Therefore every effort should be made to persist in conservative treatment, but the patient's physical and mental condition must be bolstered up constantly.

FAT DEFICIENT DIETS

To the Editor:—What are the first noticeable symptoms of fat deficiency in human beings? I have never seen any in this country, but if rationing becomes more strict we may see it here. While in Vienna I heard remarks that in World War I no fat was obtainable in Austria (and Germany?) and that that was the main reason why the armistice was signed in November 1918. I heard (in Vienna) that people at work or on the street would fall over exhausted and could not be revived unless given fat; this was given in the form of cream or butter in the early part of the war. Later on, no fats were available and so nothing could be done for such people. The doctors there attributed this sudden exhaustion to starvation in general but primarily to lack of fats. I have never read anything along the line of fat deficiency in our medical literature, but of late I have been recalling what I heard in Vienna. Can you give me something authentic on this subject? Fats are needed for making glycerin, which is needed in making explosives, so in the event of a long war we may have to face fat deficiency.

M.D., Wisconsin.

ANSWER.—The principal difficulty with the diet of people in Europe during the first world war was a lack of calories, resulting in severe loss of fat. The older people suffered from deficiency of thiamine and ascorbic acid and the children suffered from numerous vitamin and mineral deficiencies. Both children and adults had protein deficiency, as indicated by the development of "war edema." It is true that fats were low, but nobody as far as is known has produced a condition of fat deficiency in the human being. In general the diet ought to contain not less than 25 per cent of its calories in the form of fat, and it is desirable that this fat contain some of the unsaturated fatty acids, such as linoleic acid, which is found in lard and many other common fats. There is some experimental evidence which indicates that there may be a need on the part of the human being for unsaturated fatty acids, but this need is supplied by the fats that are present in ordinary foods.

INSPISSATED MUCUS ON NASAL SEPTUM

To the Editor:—A man aged 70 has a perforation of his nasal septum anteriorly, with the formation of a thin layer of jelly-like material in the area immediately behind. The material is removed with difficulty and recurs in one to two days. He has had tuberculosis, but it is quiescent; the Kahn reaction is negative. All specialists consulted have prescribed ointments which have proved ineffective. Have you any suggestions as to the cause and treatment?

M.D., Michigan.

ANSWER.—Since no mention is made of the presence of lesions on the turbinates or septum or of the presence or absence of an atrophic rhinitis one can only infer from the question that the condition described is simply one of inspissated mucus. No doubt there is a tendency to atrophy of the mucous membrane with consequent changes in the mucous glands. Tenacious secretion is quite common in such cases and will tend to accumulate and dry on the posterior margin of a perforation and the area just posterior. The treatment should be directed toward the loosening of the "jelly-like material," which can be accomplished by douching with a warm solution of sodium bicarbonate and the application of a bland nonirritating ointment such as boric acid in equal parts of petrolatum and hydrous wool fat.

ACNE, FALLING HAIR AND MENSTRUAL IRREGULARITY IN YOUNG WOMAN

To the Editor:—An unmarried woman aged 22 is the only child of a widow who shows her daughter more attention than is necessary. This girl has not worked to help support the home in the past four years; she spends a great deal of her time in bed and complains bitterly about her facial eruptions, a few acneform pustules on the chin. She has few friends and seldom goes anywhere. She recently began to menstruate twice monthly, the flow lasting three to five days with dysmenorrhea throughout the flow. There are no clots and the flow is moderate. Menses began at 14 every twenty-eight days and were always normal. There is nothing abnormal in her past history either mentally or physically. The basal metabolic rate is minus 5. The blood pressure is 118/70, the pulse 100 and regular. The heart is essentially normal. Eyes, ears, nose and throat are all grossly normal. Knee kicks are slightly exaggerated and other superficial reflexes rather normal. The abdomen is tender on deep pressure in both lower quadrants. There is no rigidity and no palpable mass. The body weight fluctuates between 127 and 133 pounds (57.6-60 Kg.). The body temperature is within normal limits. The height is 5 feet 2 inches (157 cm.). Vaginal examination reveals no discharge. The hymen is intact. Rectal examination of the pelvic organs does not reveal more than tenderness in the area of each ovary. The breasts are of normal size and consistency. The areolae are normal except for a few enlarged Montgomery follicles. The patient complains that for the past few months her hair has been falling out and that her eyes are becoming smaller. I could agree with the first, but I am not sure about the second complaint.

M.D., New York.

ANSWER.—The only recorded objective disturbances in this case are slight acne, perhaps some loss of hair and too frequent and painful menstruation. Undoubtedly there is a large psychic factor which makes the patient emphasize unduly the few acneform pustules, the falling out of the hair and the complaint about the eyes. Even though the treatment of all this patient's symptoms is generally unsatisfactory, an effort should be made to treat them. The treatment of the menstrual disorders is the most difficult. If the menses occur regularly every two weeks there need be no concern. It may be that real menstruation occurs every four weeks and that in the intervals between these menstrual flows the bleeding is associated with ovulation. This disturbance can be checked with endocrine therapy but the treatment is usually expensive and of only temporary benefit.

The patient is overweight, and thyroid medication may help some of her symptoms. In addition some form of suggestive therapy is definitely indicated. An effort should be made to have the patient get out and secure employment. Above all, some way should be found to bring her in contact with young men and women so that she may have a few close friends, especially among men. The situation should be explained to the patient's mother and her aid enlisted.

BENIGN EOSINOPHILIA OF UNKNOWN ORIGIN

To the Editor:—A man aged 55, who was born in Spain, came to me with regard to a report of a 46 per cent eosinophilia in his blood for a great many years. This finding was accidental. There is no trace of physical impairment or loss of vigor and health. Blood Wassermann and Kahn reactions have been repeatedly negative. X-ray examinations of the chest and heart have given normal results. The urinalysis gave normal results. The skin and muscles are free from deep tumors. He has been hospitalized for further study of his condition, and all tests have been negative. There has never been any illness directly attributed to the eosinophilia. There has been no local swelling or swelling of extremities. Chyluria has never been observed. Special examination of the blood day and night for microfilaria has been negative. Could you give me a possible diagnosis of a case of this kind and also the prognosis? His last hemogram was hemoglobin 101 per cent (14.7 Gm.), erythrocytes 5,090,000, leukocytes 19,150, color index 1. The differential was lymphocytes 22 per cent, eosinophils 46 per cent, basophils 0 per cent, mononuclears 1 per cent, polymorphonuclear neutrophils 31 per cent.

E. N. Boccanegra-Lopez, M.D., San Juan, Puerto Rico.

ANSWER.—There seem to be no clues in this case that would enable one to classify it among the known causes of eosinophilia. In some cases of trichinosis, eosinophilia has been reported to persist for years. A rather pronounced degree of benign eosinophilia has been observed in several members of a family (Stewart, S. G.: Familial Eosinophilia, *Am. J. M. Sc.* **185**:21 [Jan.] 1933). A study of the patient's relatives would therefore be of interest. Even after painstaking study of some patients with eosinophilia, it may not be possible to determine the cause.

As long as the patient has no complaints or abnormal physical findings and the eosinophilia is of long standing, there is no reason why this condition should give him any trouble in the future. A yearly check-up on the blood count and differential is indicated.